

**Prevalence and risk factors of peripheral arterial occlusive disease  
in adult HIV positive patients in Indian population– A hospital  
based, cross sectional study**



**A Thesis submitted to the Tamil Nadu Dr. MGR Medical University in  
partial fulfilment of the degree MS General Surgery**

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## **CERTIFICATE**

This is to certify that the dissertation titled “Prevalence and risk factors of peripheral arterial occlusive disease in adult HIV positive patients in Indian population– A hospital based, cross sectional study” is a bonafide work of Dr. S.Suraj in partial fulfilment of the requirements for the M.S General Surgery (final) examination of the Tamilnadu Dr.MGR Medical university to be conducted in April 2015.

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## **DECLARATION**

I hereby declare that this dissertation titled “Prevalence and risk factors of peripheral arterial occlusive disease in adult HIV positive patients in Indian population– A hospital based, cross sectional study” was prepared by me in partial fulfillment of the regulations for the award of the degree of MS General Surgery of the Tamil Nadu Dr.MGR Medical University, Chennai. This has not formed the basis for the award of any degree to me before and I have not submitted this to any other university previously.

Vellore

Dr. S.Suraj

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## **ABSTRACT**

### **Title of research**

“Prevalence and risk factors of peripheral arterial occlusive disease in adult HIV positive patients in Indian population– A hospital based, cross sectional study”

**Department:** General Surgery

**Name of candidate:** Dr.S.Suraj

**Degree and subject:** MS General Surgery

**Name of guide:** Dr. Sukria Nayak

**Background:** HIV has been known to cause arterial occlusive disease by atherosclerotic and non-atherosclerotic mechanisms. The underlying pathophysiological mechanisms are not well studied. There are only limited studies assessing the prevalence and risk factors of peripheral arterial occlusive disease in this population.

There are very few studies from the Indian subcontinent addressing this issue where the load of HIV is high.

As we all know, the mortality and morbidity associated with this incurable condition is high. With availability of HAART (Highly active antiretroviral therapy), patients now live longer and presence of peripheral arterial occlusive disease is emerging as a clinically relevant problem. Presence of advanced HIV disease with low CD4 count and low albumin are poor prognostic factors for operative or non-operative management of vascular disease in this

population. Rates of limb amputation with advanced disease can be higher. Detection at an early stage may help in instituting preventive measures which can help improve clinical outcome.

This study mainly aims to determine the prevalence of peripheral arterial occlusive disease in this population using clinical features and Ankle Brachial Pressure Index (ABPI). The clinical details will be recorded in a proforma.

**Methods:** A prospective observational study was conducted in the department of General Surgery and Infectious Disease Training and Research Centre (IDTRC) in the Christian Medical College, Vellore from November 2012 to September 2014. All consenting HIV positive patients eligible for the inclusion criteria were included in the study.

Methodology involved: explaining to the patient about details of study with the help of an information leaflet, obtaining informed consent and recruiting them into the study. A direct interview based on a proforma covering demography, symptomatology (assessed with help of Edinburgh Claudication Questionnaire), clinical and laboratory parameters and risk factors under study was done. Finally the primary outcome measurement using the screening tool (Ankle Brachial Pressure Index and or Toe pressure) and its documentation in the proforma was done. Data entry was done into an excel sheet. Statistical analysis was done using SPSS software. Prevalence of peripheral arterial occlusive disease and the significant risk factors for the causation of same was identified.



**Results:** A total of 403 HIV positive patients were recruited in to the study. Average age of study population was 41.45. There were 238 males and 165 females (59.1% Vs 40.1%). Claudication was reported by 19 patients (4.7%). Out of these 19 patients, 5 patients had final evidence of peripheral arterial disease. Prevalence of peripheral arterial occlusive disease (PAOD) was found to be 7.69% (n = 31). Out of these, 17 were females and 14 were males. 3 patients had >25% reduction in the post-exercise ABPI. But all these patients already had an abnormal ABPI (<0.9). Use of protease inhibitors and the duration of its use were identified to be strongly associated with causation of PAOD in this population. Traditional risk factors like diabetes mellitus, tobacco use including smoking, hypertension, and dyslipidaemia were not identified as independent risk factors for PAOD in this particular population. Duration of HIV infection, overall duration of HIV treatment and CD4 count < 300 were also found to be high risk factors for PAOD in this population, but did not attain statistical significance in multivariate analysis.

**Conclusion:** Prevalence of peripheral arterial occlusive disease in HIV positive patients is high in comparison to the general population. Traditional risk factors seem to be playing negligible role in the development of peripheral arterial occlusive disease in these patients. Protease inhibitor use and duration of its use can be strongly associated with development of PAOD in this population. Hence drug regime has to be carefully selected.

**Keywords:** HIV, peripheral arterial occlusive disease (PAOD), Ankle Brachial Pressure Index (ABPI), Toe pressure, risk factors, HAART

## **TABLE OF CONTENTS**

<b><u>TITLE</u></b>	<b><u>PAGE NO:</u></b>
Introduction	11
Aims and objectives	13
Review of literature	15
Materials and methods	55
Results	70
Discussion	99
Conclusions	107
Limitations	110
Potential for further research	113
<b><u>Annexures:</u></b>	
Patient information sheet	116
Consent form	118
Proforma	120
Bibliography	124
Data sheet	133

# **Chapter 1**

## **Introduction**

HIV has been known to cause arterial occlusive disease by atherosclerotic and non-atherosclerotic mechanisms. The underlying pathophysiological mechanisms are not well studied. There are only limited studies assessing the prevalence and risk factors of peripheral arterial occlusive disease in this population.

There are very few studies from the Indian subcontinent where the load of HIV is high. As we all know, the mortality and morbidity associated with this incurable condition is high. With availability of HAART (Highly active antiretroviral therapy), patients now live longer and presence of peripheral arterial occlusive disease is emerging as a clinically relevant problem. Presence of advanced HIV disease with low CD4 count and low albumin are poor prognostic factors for operative or non-operative management of vascular disease in this population. Rates of limb amputation with advanced disease can be higher. Detection at an early stage may help in instituting preventive measures which can help improve clinical outcome.

Our study was mainly aimed at determining the prevalence of peripheral arterial occlusive disease in this population using clinical features and Ankle Brachial Pressure Index (ABPI). The clinical details will be recorded in a proforma.

## **Chapter 2**

### **Aim and Objectives of the study**

## **AIM**

To assess the prevalence of peripheral arterial occlusive disease in adult HIV positive patients and identify other possible risk factors for the development of peripheral arterial occlusive disease in this population

## **OBJECTIVES**

### **PRIMARY OBJECTIVE**

To assess the prevalence of peripheral arterial occlusive disease in HIV positive adult patients aged  $\geq 18$  years presenting to a tertiary care hospital of India during the time period December 2012 to September 2014

### **SECONDARY OBJECTIVE**

To identify the possible risk factors for development of peripheral arterial occlusive disease in study population

## **Chapter 3**

### **Review of literature**

The acquired immunodeficiency syndrome (AIDS) is caused by Human Immune deficiency virus (HIV). It is a lentivirus belonging to retroviridae family [1]. These are single stranded, positive sense, enveloped viruses carrying an RNA genome. It causes immune system destruction by affecting various target cells and through various mechanisms [2].

First AIDS cases were reported in the United States in 1981 among intravenous drug abusers and homosexual men [3]. These men were diagnosed with *Pneumocystis Carinii* pneumonia, which was then considered a rare opportunistic infection. This infection was known to occur only in individuals with extremely compromised immunity [4]. Immediately following this incident, another set of homosexual men were diagnosed with a priorly rare cutaneous malignancy (Kaposi's sarcoma) [5]. These two incidents led to the development of various task forces being set up by the Centre for Disease Control (CDC) in USA which eventually led to the discovery of this virus.

First known case of HIV in India was diagnosed by Suniti Solomon and others amongst female sex workers in 1986 [6].

Currently about 33.4 million people are living with HIV/AIDS worldwide. It was estimated that about 2.0-3.1 million people are living with HIV/AIDS in year 2006 in India [7]. A more recent survey by National AIDS Control Organisation (NACO) of India estimated that 2.39 million Indians live with HIV/AIDS in India in 2008–09. According to NACO, the prevalence of AIDS in India in 2011 was 0.27%, which is down from 0.41% in 2002 and 0.35% in 2006 [8]. But in terms of individuals affected, India stands third in the world [9].



HIV and other lentiviruses are transmitted through various pathways including semen, blood and blood products, breast milk, vaginal secretions etc. Once the virus gains entry into the target cell, virally coded reverse transcriptase enzyme acts on the RNA genome and converts it into a double stranded DNA virus. This viral DNA, through various pathways gets incorporated into the nucleus of infected target cells [10]. After this incorporation, it can either stay latent for period of time or start multiplying to infect other cells. This depends on a various number of factors including the nutritional status of the patient.

HIV infects various cells of importance in the immune system of humans, like the macrophages, dendritic cells and helper-T cells [11]. HIV leads to a reduction in total CD4<sup>+</sup> T lymphocyte cells through different mechanisms [12, 13]

- Induction of apoptosis of normal bystander cells
- direct killing of infected target cells
- CD8+ T lymphocyte mediated killing of target cells

Two types of HIV have been identified so far: HIV-1 and HIV-2 serotypes.

HIV-1 was the virus that was initially discovered. It was initially termed as HTLV-III. This serotype of HIV is the more virulent amongst the two, and is more infective and acts as the aetiological agent for majority of infections across the globe [14].

There are various numbers of clinical manifestations of this viral infection described in humans. This includes cardiovascular, cerebral, cutaneous involvements and various types of malignancies including sarcomas and lymphomas.

Substantial numbers of opportunistic infections are also associated with HIV infection.

Opportunistic infections are defined as those infections developing in HIV patients, which are more prevalent or more severe due to the underlying immunosuppression [15].

This includes *Pneumocystis carinii* pneumonia, *Toxoplasma gondii* encephalitis, Cryptosporidiasis, microsporidiosis, mycobacterium tuberculosis, mycobacterium avium complex disease, bacterial respiratory disease and bacterial enteric disease, histoplasmosis, coccidioidomycosis, aspergillosis, cytomegalovirus (CMV) disease, herpes simplex virus (HSV) disease, human herpesvirus-8 (HHV-8) disease and varicella-zoster virus (VZV) disease [15]. Among these, mycobacterium tuberculosis is a very common opportunistic infection seen in HIV positive patients in India and neighbouring nations.

These opportunistic infections add onto the overall morbidity and mortality of patients living with HIV/AIDS. A large number of hospital admissions are also being due to these opportunistic infections. The cost involved in getting these infections treated also adds extra financial burden on an HIV positive patient.

AIDS epidemic had a large impact on the economy and health of many nations including India. AIDS related death increased rapidly during the 1980s. Average survival time after HIV infection, if left unattended is estimated to be around 9-11 years [16]. But the life span of patients living with HIV has improved in the last two decades due to the introduction of anti-retroviral agents and its effective distribution. But in parallel, the number of opportunistic infections arrived over the years. And what killed the patient after the introduction of HAART were these opportunistic infections.

Peripheral arterial occlusive disease (PAOD) is a condition which refers to the occlusion of large arteries (excluding brain, coronaries or aortic arch) by various aetiologies [17]. It is most commonly seen in the lower limbs. This can lead to various secondary effects, ultimately ending in limb loss and also in some cases, death.

202 million people were living with peripheral arterial occlusive disease across the globe in 2010. This was about 20% higher compared to 2000 estimates. About 70% of patients with PAOD were from the developing nations. About 54.8 million were living in Southeast Asian countries with PAOD [18]. Overall prevalence of peripheral arterial occlusive disease in the general population is estimated to be 1% at the age of 50 years and 3% at the age of 60 years [19]. Most of these data were based on western studies. There are limited studies in India and other subcontinent nations, which looked into the disease burden and prevalence of this disease. The Chennai Urban Population Study found an overall prevalence of 3.2% among south Indian population [20]. As the name suggests, the study was predominantly conducted in an urban setting and might not be the actual representation of the status of the disease in the country.

The most common cause of peripheral arterial occlusive disease is atherosclerosis [21, 22]. And this has remained the single most common cause across all populations.

Multiple other aetiologies are also being described, which includes [17]

- inflammatory processes (like vasculitis)
- embolism
- thrombus formation

Peripheral arterial occlusive disease (PAOD) is classified according to Fontaine stages, as described by Rene Fontaine in 1950's [23, 24]

- Stage I: Asymptomatic, incomplete obstruction of the vessel
- Stage II: Mild claudication pain in the limb
  - Stage IIA: Claudication distance >200 metres
  - Stage IIB: Claudication distance <200 metres
- Stage III: Rest pain
- Stage IV: Necrosis and/or gangrene tissues

Rutherford had recently re-classified PAOD into four grades and seven categories: [24]

- Grade 0, Category 0 - Asymptomatic
- Grade I, Category 1 - Mild claudication
- Grade I, Category 2 - Moderate claudication
- Grade I, Category 3 - Severe claudication
- Grade II, Category 4 - Rest pain
- Grade III, Category 5 - Minor tissue loss (limited ischemic ulcers)
- Grade IV, Category 6 - Major tissue loss (gangrene or severe ischemic ulcers)

Typically, endovascular or surgical interventions are reserved for Class III and higher.

Risk factors for PAOD are multiple. Major among them are: [25]

- Old age (especially >50 years)
- Male sex
- Smoking or use of tobacco in any forms
- Diabetes mellitus
- Hypertension
- Dyslipidemia
- Obesity (BMI >30.0)
- History of prior cardiovascular events
- Family history of vascular disease/events

Potential risk factors for PAOD include elevated levels of the following [26]:

- Homocysteine
- Lipoprotein-a
- C-reactive protein (CRP)
- Fibrinogen
- Plasma viscosity
- Apo-lipoprotein B

## **Smoking**

Tobacco in any form has been identified as the single most important modifiable risk factor of PAOD. Smoking was identified as the leading modifiable risk factor for arterial occlusive disease after the Framingham study found out a significant longitudinal association between it and PAOD [27]. Smoking was also found to be responsible for major number of the PAOD cases in the National Health and Nutrition Examination Survey [28]. Various quality of life studies have shown a superior life quality for non-smokers living with PAOD than smokers [29]. Studies from Asia also have identified that PAOD is a common disease among geriatric population with almost 40% of them remaining asymptomatic. Smoking was identified as the major risk factor for PAOD in this study too, with a two-fold increased risk of PAOD among smokers compared to non-smokers [30].

Increased risk of PAOD is also associated with the number and duration of smoking [18]. There is a three-fold higher risk of developing PAOD in patients who have smoked for less than twenty five years, compared to non-smokers. Among those who have smoked for 25 years or more, this risk increases to about five-fold [31].

In PAOD patients who smoke, the chance of being having another cardiovascular risk factor is also high [28]. Among diabetics, the risk of PAOD is increased by a further 50% if the patient had history of tobacco use in some form [26, 27].

Smokers have about tenfold increase in relative risk for PAOD in a dose-related effect and they also tend to develop more PAOD rather than coronary or cerebro-vascular events [27]. Smokers have also been found to have greater risk of developing symptomatic as opposed

to asymptomatic PAOD, in particular an increased risk of intermittent claudication. They also experience symptoms about 10 years earlier than the non-smokers [32].

About 80%-90% of lower extremity peripheral arterial occlusive disease patients are found to be current or reformed smokers [18, 26]. Observational studies have found that the risk of death, myocardial infarction, and amputation is substantially greater among smokers with PAOD. Success rates of lower extremity interventional procedures (open or endovascular) for PAOD are low if the patient continues to smoke [25].

Environmental exposure from second hand smoke also leads to endothelial damage, which acts as precursor to atherosclerosis and thereby to the development of PAOD.

There are different mechanisms through which smoking leads to the development of peripheral arterial occlusion:

All tobacco products contain a large quantity of nicotine. Once a tobacco product is consumed, especially when smoked, nicotine gets rapidly absorbed into the circulation. This stimulates the release of various neurotransmitters (epinephrine and norepinephrine) from their storage cells. These neurotransmitters bind to vascular smooth muscle cell receptors resulting in varying degrees of vasoconstriction. This effect is usually brought into equilibrium by the release of various vasodilators stored predominantly in the vessel wall (like nitric oxide). But in tobacco users especially in smokers, there is a loss of this equilibrium due to reduced production of vasodilatation agents. This leads to chronic repeat episodes of vasoconstriction [18].

These effects have been demonstrated in various quantitative studies as well. In non-smoking healthy adults, the usual amount of vasodilatation which happens in the larger arteries of upper (brachial artery) and lower limb (femoral artery) are 11% and 4% respectively. This is reduced to 4% and 0% respectively in young otherwise healthy smokers [33].

Carbon monoxide in tobacco smoke has a greater affinity to haemoglobin than oxygen. So whenever a person smokes, the levels of carboxy-haemoglobin in the blood rise in comparison to oxyhemoglobin. This leads to oxygen deprivation at the tissue level. Carbon monoxide also increases the viscosity of blood, thereby hindering the available oxyhemoglobin reaching the tissues [18]. The net result of all these is tissue hypoxia. And when it happens in a chronic setting, it ultimately leads to tissue ulceration and/or gangrene.

Smoking also results in a hypercoagulable state, thereby helping in the formation of clots in the vascular system [18].

Smoking can also lead to arterial occlusion in an indirect way by promoting atherosclerosis. This is initiated by endothelial damage secondary to the deleterious effects of various toxic chemicals in the tobacco. Damaged endothelial cells promote transfer of LDL cholesterol across the vessel wall, resulting in the formation of lipid plaques [34].

Tobacco, particularly smoking also reduces the levels of the HDL cholesterol, which is considered as “good cholesterol” [34]. Tobacco smoke also can cause derangements in



other components of the lipid profile including a rise in triglyceride levels and total cholesterol levels.

A particular disease in India, where smoking is a strong risk factor for development of PAOD is Buerger's disease or Thrombangitis Obliterans (TAO). TAO affects the small and medium-sized blood vessels of the body including both arteries and veins [35, 43]. Tobacco in any form can be the risk factor and only about 5% of affected are non-smokers [18, 35]. This disease is commonly seen in young male patients who smoke.

Tobacco, particularly smoking initiates an immune response in susceptible persons or unmasks an underlying coagulation defect. This leads to an inflammatory reaction of the vessels including veins, arteries and even the adjoining nerves. This is classically described as the "pan arteritis" of Buerger's disease [18, 35, 43].

Any intervention aimed at smoking cessation is vital in patients with Buerger's disease. This is due to the aetiological contribution of tobacco in the development of this disease. And on the same note, the outcome of patients who continues to smoke is grave even after the institution of other therapeutic tools [18, 35].

### **Diabetes mellitus**

Risk of developing PAOD among diabetics is related to the severity and duration of diabetes mellitus. Diabetic patients have about 2-4 times increased risk of developing PAOD compared to a non-diabetic. Diabetics who smoke have a greater risk of developing PAOD, and runs about 30% risk of an amputation in the next five years [26].

Diabetes causes endothelial cell function and vascular regulation abnormalities [26].

Most important pathway by which diabetes affects the endothelium is by derangement of nitric oxide bioavailability. Nitric oxide act as a vasodilatation agent and it also prevents leukocyte-vascular wall interaction. It also prevents vascular smooth muscle cell proliferation and migration. Peripheral activation of platelets is also prevented by nitric oxide. Hyperglycaemia blocks the function of e-NOS which is located in the vascular endothelium. This leads to the production of reactive oxygen molecules, which impairs the vasodilatory equilibrium in the endothelium. This oxidative stress is further amplified since the vascular endothelial cells (in comparison to other cells in the body) lack the down regulation of glucose transport triggered by high blood sugars [26].

Insulin resistance also plays a major role in the loss of nitric oxide homeostasis [36]. One of the important mechanism by which insulin resistance disrupt the nitric oxide homeostasis is by the release of excess free fatty acids (FFAs). Free fatty acids in turn cause various toxic effects on vascular homeostasis, ultimately resulting in loss of nitric oxide homeostasis. This includes [37]:

- formation of reactive oxygen molecules
- protein kinase C (PKC) activation in the endothelium
- Inhibition of phosphatidylinositol-3-kinase

Local rise in multiple pro-inflammatory substances (activator protein 1, nuclear factor-  $\kappa$ B) combined with loss of nitric oxide homeostasis affects various leukocyte functions. This includes enhanced neutrophil chemo taxis, more number of adhesions, and transmigration across the cell and transformation to “foam cells”. The process of transformation to foamy cells is further enhanced by a higher oxidative stress at near the vascular endothelium [37]. Foam cell transformation is regarded as the earliest precursor cell of vascular atherogenesis.

### **Dyslipidaemia**

Dyslipidaemia is well recognised as a major risk factor for any cardiovascular diseases including PAOD. Low HDL cholesterol, high LDL cholesterol, elevated total cholesterol and triglyceride levels have been correlated well with development of PAOD.

Dyslipidaemia correction by life style modifications and/or lipid lowering drugs has been found to reduce the rates of major cardiovascular events in the life term [25]

### **Hypertension**

Hypertension is associated with an increased risk of developing PAOD, as well as in the further development of other major cardiovascular events [25]. Hypertension alone increased the risk of intermittent claudication for about 4 and 2.5 fold in men and women, respectively [25]. Hypertension is commonly an associated risk factor in smokers and diabetics, and the combined effect of all these can be detrimental.

## Obesity

Obesity was strongly associated with elevated inflammation markers like C-reactive protein and fibrinogen, which are predictors for active atherosclerosis.

The prevalence of metabolic syndrome was found to be more among PAOD patients than other cardiovascular diseases. It was 58% in PAOD patients, 47% in abdominal aortic aneurysm (AAA) patients, 43% in cerebrovascular disease patients and 41% in coronary disease patients [38]. Each 5-unit increase in body mass index among adult Israeli men resulted in about 24% greater risk of intermittent claudication among adult Israeli men, adjusted for smoking status and number of pack years [39].

Body mass index and Waist to hip ratio are the two commonly used tools to define obesity. A body mass index of  $>30$  is defined as obesity [25].

Obese patients were found to have a greater oxidative stress. This leads to decreased nitric oxide bioavailability in the vascular endothelium. This in turn leads to endothelial dysfunction & vasoconstriction, and thereby to the development of PAOD.

In the Framingham Heart Study, body mass index was closely associated with systemic oxidative stress, as obtained by biochemical tests. A decrease in the function of nitric oxide would also predispose to other cardiovascular disease risk factors such as hypertension [40]

A carefully taken detailed clinical history and thorough physical examination is required in the identification of patients with possible PAOD. History should be taken in such a way so as to include:

- risk factors
- symptoms of claudication & claudication distance
- rest pain
- varying degrees of functional impairment/tissue loss
- details of prior interventions
- details of prior cardiovascular events
- symptoms pertaining to other vascular system involvement

Alternative causes for pain in the leg need to be carefully excluded. A thorough walking history will help us elicit classic symptoms and its variations.

The classical symptom of peripheral arterial occlusive disease is the “intermittent claudication pain” [21, 22]. Claudication is derived from Latin word “claudicatio”, which means “to limp”.

Claudication pain is defined as a reproducible pain experienced in the muscles of calf/thigh/buttock, brought in by exercise (typically walking) and relieved immediately by rest [22].

It is classified by Boyd into four categories as described below [41]:

#### **Boyd's classification of claudication**

Grade I – Patient develops pain on walking. If he continues to walk, pain disappears.

Grade II – Patient develops pain on walking. If he continues to walk, pain persists. But the patient can still walk with efforts.

Grade III – Patient develops pain on walking. The pain compels the patient to take rest.

#### **Characteristic features of claudication pain [42]**

1. Claudication pain is brought on by exercise
2. Claudication pain is relieved at rest
3. Claudication pain is a cramp like pain felt over the musculature
4. Claudication pain is almost always reproducible

#### **Importance of site of claudication pain [42]**

Site of claudication pain is an indicator to the level of arterial occlusion;

SITE	LEVEL OF OCCLUSION IN THE ARTERY
Gluteal	Iliac
Thigh	Femoral
Calf	Popliteal
Foot	Tibial

PAOD patients present with a large spectrum of symptoms, ranging from asymptomatic, intermittent claudication, rest pain, and non-healing ulcers and/or gangrene.

A thorough physical examination should be carried out. This includes:

- Documentation of vital parameters
- Body mass index or waist to hip ratio
- Documentation of all peripheral pulses and its strength.
- Checking for bruits in the common areas
- Visual inspection of the foot and hands for dependent erythema, pallor on elevation, absence of hair growth, dystrophic toe nails, and cool, dry, fissured skin
- Look for fissures, ulcerations, and presence of infections in the foot
- Examination of cardiac system especially looking for murmurs

Peripheral pulse documentation is of greater importance in patients suspected of having PAOD, and also in those patients without PAOD, but with a risk factor for the same (viz.DM). The character of pulse also needs to be noted (strong Vs weak Vs absent).

Pulse documentation can have high degree of inter-observer variability, thereby resulting in false positive and false negative results. Also it has to be remembered that about 8%

patients can normally have an absent dorsalis pedis artery pulsation and about 2% can have absent posterior tibial pulsations [26]. But absent pedal pulses felt by an experienced hand should always raise the suspicion of PAOD in any patient [26].

But among those with PAOD, about 50% do not demonstrate any symptoms or have atypical symptoms, about 30% have “intermittent claudication”, and the rest have more severe forms of vascular occlusion [43]

History and physical examination may miss those asymptomatic patients which forms a major number of patients living with PAOD.

Patients are usually screened for the disease when they present with the symptoms or if the disease is clinically suspected (Eg: long standing diabetes). In Indian scenario, patients often present in a complicated stage, which makes the limb salvage low. Hence it is very important to diagnose the disease at the earliest so that the interventions can be instituted at the earliest.

Lower limb ischemia can be classified as functional or critical [44]. Functional ischemia develops when the arterial blood flow is normal at rest but gets deprived during an exercise. This clinically presents as intermittent claudication. Critical limb ischemia is developed when this reduced blood flow results in reduced tissue perfusion at rest. This is defined by the presence of rest pain or trophic changes in the peripheries. Hence it is very important to differentiate between these two entities since the therapeutic indications and final prognosis of patients with PAOD is determined by this [44].



Lower limb ischemia can also be classified as acute or chronic [42, 44].

Acute limb ischemia occurs due to sudden decrease in the blood flow to a limb, resulting in a potential danger to the viability of the peripheral tissue, and in some cases, threat to life as well. Limb hypo perfusion results in hypoxia which leads to acid base disturbances especially lactic acidosis and dyselectrolytemia. These in turn endangers various systemic functions of the body. Successful reperfusion may result in the release of highly toxic free radicals, further compromising these critically ill patients.

Two common causes of acute limb ischemia are thrombosis or embolism [44, 45]. Embolic problems result in a severe ischemia in comparison to thrombosis, as the embolus typically lodges in a "virgin" vascular bed with no collateral circulation. On the contrary, thrombosis mostly occurs in those vessels which already harbour atheromatous narrowing, that have triggered the development of collateral circulation. The presence of these collaterals reduces the severity and rapidity of symptom development in such patients, especially when the "narrow" vessel advances to an "occluded" vessel.

It is often difficult to distinguish an embolic occlusion from a thrombotic occlusion. However there were few factors which point towards a possible embolic occlusion [42, 44]:

- acute onset
- history of embolic event
- no prior history of intermittent claudication
- known source of embolus, such as cardiac
- normal pulses and doppler studies in the unaffected side

Generalized atherosclerosis leading onto thrombosis is the most common aetiology for acute occlusions of peripheral vasculature. The superficial femoral artery is the most common site of atherosclerotic narrowing. Aggressive use of bypass grafts has resulted in a greater number of patients presenting with acute limb ischemia.

The clinical presentation is considered to be acute if it occurs within 2 weeks after symptom onset. Symptoms develop over a period of hours to days [42].

Classical description of patients with acute vascular ischemia is represented by the "six Ps": pain, pallor, paralysis, pulse deficit, paraesthesia, and poikilothermia [42].

Severity of acute limb ischemia is classified according to Rutherford classification [45, 46]:

#### **Rutherford Classification of Acute Limb Ischemia**

Category I: Viable - no immediate limb threat

- Sensory deficit – nil
- Motor deficit – nil
- Arterial doppler signals present, but typically monophasic + venous doppler signals

Category IIA: Marginally threatened

- Sensory deficit – minimal (e.g. toes involved)
- No motor deficit – nil
- Arterial doppler signals absent + venous doppler signals present

#### Category IIB: Immediately threatened

- Sensory deficit with rest pain
- Motor deficit - Mild to moderate
- Arterial doppler signals present + venous doppler signals present

#### Category III: Irreversible (major tissue loss with permanent nerve injury)

- Sensory deficit – severe with complete anaesthesia
- Motor deficit - Severe with paralysis or rigor
- Arterial doppler signals absent + venous Doppler signals present

Mortality rate and complications among patients who present with acute limb ischemia are high. Despite urgent revascularization interventions, amputation rate among hospitalised patients range from 10 to 15%. 1 year mortality rate after initial presentation is about 15 to 20%, mostly from the underlying conditions that predisposed to acute limb ischemia [44].

The final impact of PAOD can be assessed by its rate of progression, whether the patient is symptomatic or asymptomatic and the presence of additional cardiovascular events associated. Majority of patients may remain stable with respect to the peripheral symptomatology during this five year period. About 20% develop nonfatal major cardiovascular events (coronary or cerebral) and about 30% eventually die during the next five years after the diagnosis of PAOD [47]. About 27% of patients with PAOD demonstrate symptom progression over a 5-year period. About 4% end up in varying degrees of limb loss over the same period. Those patients who have critical limb

ischemia, the outcomes are not good. About a third will end up with an amputation(s) and about a fourth will die within next 6 months [43, 47].

Patients with peripheral arterial occlusive disease (PAOD) has six times increased risk of death from coronary artery disease and three times increased risk of death from any other cause [48]. PAOD is a predictor of development of future cardiovascular mortality and morbidities including cerebrovascular accident and myocardial events [22, 25].

About 63% of symptomatic PAOD patients have polyvascular disease. PAOD patients over the age of 50 have a 68% and 42% incidence of coexistent coronary artery disease and cerebrovascular events respectively [26].

In view of all these factors, the early diagnosis and intervention of peripheral arterial occlusion is extremely important; both with respect to the reduction of morbidity and mortality associated with the disease and also other cardiovascular diseases.

Sensitivity and specificity of clinical examination in picking up peripheral arterial occlusive disease is low [25, 49]. In the absence of a femoral bruit, the presence of all lower limb pulses predicts a normal ABPI with good sensitivity. Most reliable finding in the palpation of pulses which point towards the presence of PAOD is the absence of posterior tibial artery pulsation. This has a specificity of about 70% and a sensitivity of about 90% for identifying lower extremity peripheral arterial disease [49].

Patients with an abnormal vascular examination should undergo ankle brachial pressure index measurement. Absence of dorsalis pedis and posterior tibial artery pulsations in any patient, especially when associated with a femoral bruit should raise high suspicion for PAOD, and an ABPI should be ordered in such patients.

There exists a large inter-observer variability in the clinical examination especially with respect to the palpation of peripheral pulses. Hence various non-invasive, easy to perform, cost effective modalities have been developed over the years. These modalities are being employed in as screening tools in various studies on PAOD.

Having a claudication questionnaire with good sensitivity combined with a non-invasive test of reasonable sensitivity, and a good clinical examination can diagnose most of symptomatic and many asymptomatic peripheral arterial occlusive disease [25].

WHO/Rose's questionnaire was the traditional questionnaire used in the past for identifying claudication. It was developed in 1962 for use in large epidemiological surveys. Rose's questionnaire was found to have a sensitivity of 60-68% and specificity of 90-100% in large epidemiological studies [50]. Owing to the low sensitivity of this, the requirement of another screening questionnaire arose. Hence a modified version of it was developed – The Edinburgh Claudication Questionnaire (ECQ) (included as part of proforma).

The ECQ was developed and validated as part of the Edinburgh Artery Study [50] which recruited 300 participants presenting with leg pain. This has 91% sensitivity and 99% specificity for identifying true claudication which is considered the classical symptom of peripheral arterial occlusion [50]. Since

then, this questionnaire has been largely employed in various studies on PAOD across the globe. One drawback of ECQ lies in the fact that it helps us in identifying only the symptomatic PAOD patients. About 50% patients with PAOD might not have any symptoms. Hence this questionnaire needs to be accompanied by a sensitive screening tool so as to detect the asymptomatic PAOD patients as well.

Angiography is considered the gold standard for diagnosis of peripheral arterial occlusive disease. CT and MR angiography are the widely used modalities. CT angiography has about 95% sensitivity and specificity in diagnosing significant stenosis in the vascular system [51]. CT angiography also gives a clear picture of the vessel wall and its adjoining structures. It can detect in detail about the plaque characteristics, presence or absence of vessel wall calcification and ulceration. Details about the presence of a thrombus can also be obtained. In patients who have an in-situ stent, CT angiography can help detect restenosis and “stent fractures” [52].

Major drawbacks of CT angiography are the use of contrast and thus the invasiveness. In patients with renal failure or contrast allergies, one needs to be careful in ordering CT angiography as the diagnostic tool. Also in comparison to MR angiography and duplex studies, there is radiation exposure and its hazardous effects including the future risk of malignancy. CT angiography is intermediate in cost compared to MR angiography and is costlier than arterial duplex [52]. But nowadays most tertiary care centres harbour a CT machine making it possible to obtain angiography.

MR angiography has many benefits over CT angiography for obtaining the peripheral arterial tree details. Most important of all these is the absence of radiation exposure. Risk of contrast induced nephropathy is low in comparison to other angiographic modalities which use iodinated contrast

agents [53]. The sensitivity and specificity of MR angiography in detecting arterial stenosis reaches about 80–90% range [54].

Performing angiography is costly, time consuming, cumbersome and invasive. Hence in many populations, especially in developing countries where people are not affordable, it becomes impractical to use these modalities for a community screening program. They can be used to confirm disease in clinically proven cases (absent or diminished pulses) or to diagnose clinically strongly suspected patients (classical intermittent pain/rest pain) with normal ABPI.

Arterial duplex scan is another modality which can be used to confirm the presence of PAOD. In addition to vascular anatomic details, it also provides information about the flow details within the vessels [55]. It can also give information about the level and extent of occlusion. Another greater advantage is the non-invasiveness. It has been widely used as a screening tool to decrease the necessity for invasive modalities especially in low income settings. It is relatively cheap and can be performed in multiple settings. The sensitivity and specificity of duplex scan in diagnosing arterial stenosis ranges between 70 and 90% in various studies. Additional advantage of arterial duplex is its usefulness during an interventional procedure to assess the response [55]. But still angiography remains the gold standard.

Major advantages of duplex scan compared to angiography are its non-invasiveness and relatively lower cost. Even though the comparative cost is less than that for an angiography, it still remains costly for a patient in the developing/underdeveloped countries. Hence using this as a screening tool for screening in Indian population is out of question as well.

Most of the studies which had assessed PAOD used Ankle Brachial Pressure Index (ABPI) as the screening tool [56]. This is a simple, relatively cheaper and non-invasive method of screening for presence of PAOD. It can be done using a hand held Doppler machine and requires only a minimal training. This can be performed as an outpatient office test as well. Due to these advantages, this has become the standard screening tool for identifying PAOD in all parts of the world including our country.

Ordinary stethoscope was used in the initial days to measure blood pressures for calculation of ABPI. But it was found to be less accurate than Doppler measurements. Hence the trend has changed over the years to the use of a Doppler machine in determining the blood pressures so as to help in calculation of a more accurate ABPI [57]

Patient is made to rest for a period of about 5-10 minutes. Systolic blood pressures of both the brachial arteries are measured with the help of a standard sphygmomanometer and a hand held Doppler machine. Similarly the systolic blood pressures at the ankles are also measured separately for each lower limb. Cuff should be ideally placed about 2.5cm above the ante-cubital fossa in case of arm and about 5cm superior to the medial malleolus for the ankle pressures. A clear arterial pulse signal should be obtained with the help of the Doppler probe before initiating the test. The cuff is then slowly inflated. The pressures at which the arterial Doppler signals disappear are noted. The cuff is further inflated for another 20 mm Hg. This has to be maintained for few seconds after which slow deflation of cuff is initiated. The blood pressure at which the Doppler signals are re-heard is considered as the systolic blood pressure in that vessel/limb [57, 58].



The ankle-brachial pressure index (ABPI) is then calculated by dividing the higher of the two systolic blood pressures at the ankle (posterior tibial & dorsalis pedis) by the higher of the two brachial systolic blood pressures. ABPI is thus calculated separately for each leg [57].

ABPI = Highest systolic blood pressure in one side foot [PTA or DPA]/ Highest systolic blood pressure among the brachial artery

PTA = Posterior tibial artery

DPA = Dorsalis pedis artery

Diagnosis of peripheral arterial occlusive disease is made when ABPI <0.9 [47, 58]. ABPI below 0.9 indicates PAOD with 95% sensitivity and 100% specificity for picking up clinically significant occlusive disease, in comparison to angiography which is considered the gold standard [59]. Various other studies have shown that the sensitivity and specificity of ABPI ranges from 79-95% and 90-100% respectively [25, 56].

It is shown that the sensitivity of ABPI can further be increased by adopting a post exercise ABPI measurement [22, 25, 60]. During exercise, there is an enhancement in the blood flow to the tissues. This excess flow has to happen across a fixed stenotic segment of the vessel, which prevents this from happening. Hence there is a fall in the ankle pressures, which is reflected in the measurement of ABPI as well [57]. This is important in identifying mild forms of occlusion which unmask only during an exercise manoeuvre. A post exercise reduction in ankle brachial pressure index to abnormal value (<0.9) is considered as significant with respect to occlusion. Certain studies also consider a fall in ABPI to >20-25% as significant for occlusion as well [74]. If the patient develops leg symptoms, especially pain during these exercise manoeuvres, it provides further evidence to the

vascular origin of symptoms [57]. Various exercise modalities are described in literature. No standard recommendation is available for the same. Some included tread mill based tests and others included simple exercise regimes likes walking in the corridor and heel raise test [22, 60]. The adequacy of an exercise regime is also not standardised.

Severity of peripheral arterial occlusive disease can also be defined using ABPI. An ABPI of  $<0.4$  is defined as “critical limb ischemia” especially if associated with tissue loss or rest pain [42]. Critical limb ischemia is of significance in the fact that it needs emergent intervention from a trained vascular specialist.

ABPI value can also correlate with the severity of PAOD [42, 25]:

Normal: 0.91–1.30

Mild obstruction: 0.70–0.90

Moderate obstruction: 0.40–0.69

Severe obstruction:  $<0.40$

It is known that, patients with severely calcified wall of arteries, even a higher systolic blood pressure won't be able to compress the vessel wall. Hence ABPI will be shown erroneously high [25]. This cut off has been repeatedly being changed and used in various studies ranging from  $>1.1$  to  $>1.4$ . Two common examples for the same are chronic kidney disease and long standing diabetes mellitus. Toe arteries are usually compressible even when it's impossible to compress the pedal

arteries. Hence in these patients with non-compressible pedal arteries, toe pressures or toe-brachial index can be obtained instead of ankle brachial index to confirm the diagnosis of peripheral arterial disease [25].

Toe pressures are measured by measuring the great toe blood pressure with the help of a digital blood pressure cuff and a Doppler probe or a plethysmographic flow sensor. The toe-brachial index is calculated by dividing the toe blood pressure by the higher of the two brachial artery pressures [57]. TBI of  $<0.7$  and/or toe pressure of  $<50$  mm Hg is taken as abnormal for diagnosis of PAOD [25, 57].

Vascular specialists could also use segmental pressures, Doppler waveform analysis, pulse volume recordings, or ABPI with duplex ultrasonography to document peripheral arterial occlusion and its possible anatomic location [25].

Problems and errors encountered during the ABPI measurement includes:

- Size of the cuff being not ideal for the patient (small cuff in a fatty or edematous leg) leading to wrong values
- Placement of blood pressure cuff in the wrong place (ideal location being about 5cm above the medial malleolus) usually leads to erroneously higher ankle pressures.
- Repeated inflation or prolonged inflation of blood pressure cuff leading to an erroneously low ankle pressures.
- Rapid deflation of the blood pressure cuff.

- Improper positioning of the patient (erroneously high value can be obtained if the ankle pressures are obtained with the leg in a dependent posture)
- Difficulties encountered in patients with an irregular pulse, leading to erroneous values.
- Effect of central systolic blood pressure : normal range of ABPI could be affected by the central systolic blood pressure of the patient at the time of examination
- Calcified vessels as mentioned earlier

One of the recent meta-analysis showed that low ABPI (marker of PAOD) itself is an independent risk factor for cardiovascular mortality alongside the traditional Framingham risk factors [59]. Another prospective study of more than thousand random patients aged between 50-74 years re-emphasised similar relationship between a low ABPI and risk of future cardiovascular deaths [62]. This study found that in patients with evidence of symptomatic PAOD ( $<0.9$  ABPI), the relative risk of cardiovascular death was 2.67. The relative risk in asymptomatic patients was found to be between 1.74 and 2.08. There are other multiple studies where in a low ABPI  $<0.9$  has been demonstrated to carry high chance of increased cardiovascular mortality and morbidity [25, 63, 64, 65, 66].

There is a good inter-observer reliability in the measurement of ankle brachial index, when done by trained persons ( $\kappa$ -value of 0.77-1.0).

Intra-observer variability in various studies stands between 7.3 to 12% [67].

Another important aspect of ABPI value which one needs to keep in mind is a higher than normal ABPI value. Importance given to such a value in the earlier days was very low. But off late studies have repeatedly proved that higher than normal ABPI also is a predictor for an increased all-cause cardiovascular mortality in future [68].

ABPI has emerged as an important screening tool for assessing peripheral arterial occlusive disease across the globe. In countries like ours, where health care affordability is poor, this stands as a relatively cheaper tool to assess for the presence of peripheral arterial occlusive disease (PAOD).

The vascular manifestations of HIV are well described in literature. HIV vasculopathy was first described as an entity in 1987 [69]. Three clinical syndromes are described with respect to HIV and vascular system [70].

- atherosclerotic occlusive disease
- non-atherosclerotic disease (vasculites and aneurysms)
- prothrombotic states

Among these, atherosclerotic disease is the commonest and vasculitis is the least common (about 1%) [71].

Characteristics of HIV associated vasculopathy differs from general population in the following ways [72]:

- young age of onset
- less prevalent traditional risk factors
- more advanced disease at presentation
- Extensive disease with poor peripheral run off

- higher rate of complications especially wound and graft related
- Increased perioperative and postoperative mortality and morbidity

Surgical outcome has been found to be largely independent of the CD4 values and hence no patient should be denied an operation based on low CD4 count [70]. Treatment options have to be individualised. Strict vascular surgical principles should be followed while managing HIV-associated occlusive vasculopathy.

Various pathophysiological mechanisms leading to vasculopathy is being studied in HIV patients. Most plausible link is thought to be the endothelial dysfunction [73]. Multiple other links described are [70, 74]

- immune suppression
- direct viral injury of endothelium
- vasculitis
- worsened metabolic parameters by HAART therapy

Among these, endothelial injury mediated mechanism stands out as the leading pathophysiological mechanism.

Endothelial injury plays a major role in the development of cardiovascular and inflammatory pathologies. This has been described in Human Immunodeficiency Virus (HIV) infection as well [75]. It is proved that, various endothelial cells in the body like hepatic sinusoidal cells, umbilical venous endothelial cells, marrow stromal endothelial cells or cerebral capillary endothelial cells, offer variable permeability for HIV. Soluble adhesion molecules and

procoagulant proteins, which act as markers of endothelial activation, have been found in excess in HIV infected patients.

Viral entry into endothelial cells may occur via various mechanisms. CD4 antigen, galactosyl-ceramide receptors and chemokine receptors mediated entry is well described in literature.

Cytokines secreted in response to the mononuclear or adventitial cell activation by HIV virus or by the action of the secreted HIV-associated proteins (gp 120 and Tat on viral replication) can also help in virus penetration of endothelial cells. Inflammatory cytokines and viral proteins can act in synergy leading to endothelial injury. These dysfunctional or injured endothelial cells potentiate inflammation, tissue injury and tissue remodelling, and thereby accentuate the development of various cardiovascular diseases including peripheral arterial occlusive disease [75].

Other abnormalities predisposing to a procoagulant state have also been detected in HIV patients. This includes antiphospholipid antibodies, lupus anticoagulant, increased von Willebrand factor (vWF), deficiency in protein C and S, AT-III (antithrombin) and heparin cofactor. Factors such as opportunistic infections and HIV associated neoplasms may also contribute to the procoagulant state [76].

HAART stands for highly active anti-retroviral drugs. It has formed the centre core of treatment for HIV positive patients. It has helped reduce the morbidity and mortality of HIV positive patients. It decreases the total burden of HIV, maintains good immune system

function and helps prevent HIV associated opportunistic infections [77]. In India, these drugs are provided free of cost through various ART centres for the needy.

There are different classes of drugs, which are usually combined to treat HIV infection. This combination can be termed anti-retroviral therapy (ART), combination anti-retroviral therapy or highly active anti-retroviral therapy (HAART). The decision on which dual NRTI combination or 'backbone' to use, and which agent to combine it with, is dependent on numerous factors, including CD4 count, HIV viral load, drug toxicities and interactions, pill burden and viral resistance [77, 78]. Commonly used combinations include 2 nucleoside reverse transcriptase inhibitors (NRTI) as a "backbone" along with 1 non- nucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitor (PI) or integrase nuclear strand transfer inhibitors (INSTI) as a "base" [78]. This combination therapy helps prevent drug resistance by suppressing HIV replication. It does this by reducing the pool of spontaneous resistant mutations. Combinations of anti-retroviral agents create multiple obstacles to HIV replication and reduce the possibility of a superior mutation. If a mutation that provides resistance to one of the drugs in the combination arises, the other drugs continue to prevent the multiplication of that particular mutant [77, 78]. In this way HAART become an effective model to treat HIV infection.

ART drugs have various side effects some of which could be serious. Prior to the introduction of HAART, it was recognised that HIV infection itself caused dyslipidaemia [79]. Declines in total cholesterol, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) have been shown in men who seroconverted from HIV-



negative to HIV-positive [81]. HIV-infected, untreated patients (particularly those with more advanced disease) are more likely to have low total, LDL-C and HDL-C and elevated serum triglyceride (TGs) than HIV-negative controls [78, 81, 82 ], with lower HDL-C concentrations associated with higher viral load and more prolonged duration of infection.

Protease inhibitors are of concern for vascular surgeons and Cardiologists. Many ART drugs have dyslipidaemia properties. Use of protease inhibitors has been associated with hypertriglyceridemia and hypercholesterolemia. Ritonavir is a potent inhibitor of the cytochrome P450 enzyme system used in the treatment of HIV/AIDS as part of HAART [84]. Various trials in healthy volunteers have shown it to have dyslipidaemic properties. Triglyceride and LDL-cholesterol levels were shown to increase by 26% and 16% respectively after about 2 weeks of treatment [84]. When used in voluntary subjects, in combination with other PIs, an enhanced dyslipidaemic property was demonstrated at about 4 weeks into the treatment [84, 85]. Effects similar to these were also demonstrated in studies comprising of HIV infected patients as well [77]. Dyslipidaemic property varies based on the type of protease inhibitors used. Atazanavir and Darunavir are relatively newer protease inhibitors which have been found to have negligible dyslipidaemia properties [77].

Hypertriglyceridemia could be a response to systemic inflammatory reaction in HIV positive patients. IFN-alpha is a marker of systemic inflammation, which is found in excess in HIV infected patients. In HIV infected untreated subjects, there exists a good correlation between IFN-alpha levels and triglyceride concentrations and triglyceride clearance time [77].

Use of protease inhibitors can also be associated with other metabolic derangements in HIV patients. This includes insulin resistance, metabolic syndrome and risk of future cardiovascular events including myocardial infarction [56, 86, 87]. More than just the use, it's the prolonged duration of treatment with these drugs which can cause persisting metabolic derangements [56]. Hence it is very important to choose ART regime in a patient with PAOD or other cardiovascular morbid illnesses.

Having known all these in general population; peripheral arterial occlusive disease is a least studied entity in HIV patients. There are only limited studies which had assessed the prevalence of same in this group especially from India. Studies have found various risk factors (few different from the traditional risk factors) which independently contributed to the occurrence of PAOD in HIV patients [56].

Prevalence of PAOD in HIV patients using ABPI as the screening tool in limited studies varied from 0.9% to 22.4% [56].

The Swiss HIV cohort study [74] recruited 92 consecutive HIV positive patients. Claudication was reported by 15.2% of the patients. All patients were assessed for presence of PAOD using ABPI as the tool. PAOD was found in 20.7% of the patients. Among these, 9.8% had an abnormal ABPI ( $<0.90$ ) at rest, and 10.9% had significant post exercise reduction in ABPI to  $>25\%$ . 84.2% of those with PAOD were investigated further with arterial duplex scan, all of whom had atherosclerotic occlusions of the lower limb arteries.

Age, diabetes, smoking, and low CD4 counts ( $<200$ ) were identified as independent predictors of PAOD in this population.

The study concluded that the prevalence of symptomatic and asymptomatic PAOD is high among HIV population compared to general population. This study was important in the fact that; it used post exercise ABPI also, which helped them diagnose patients with mild forms of occlusion.

Another study by Palacios et al [88] recruited HIV positive subjects for assessment of PAOD with a control group. 82.8% patients were males and 17.2% were females. ABPI was used as the screening tool in this study too.

The prevalence of PAOD was found to be significantly greater among the HIV positive patients in comparison to HIV negative patients (10.2% vs 1%). HIV-group in comparison to controls comprised of - more smokers (30.3% vs 46.5%), those with higher BMI (24.8 kg/m<sup>2</sup> vs 27.7 kg/m<sup>2</sup>), DM (31.3% vs 12.2%), higher proportion of dyslipidaemia (69.4% vs 36.7%), and higher cardiovascular risk (29.5% vs 13.4%) as calculated by Framingham's criteria.

Study by Olalla et al [56, 89] recruited 147 HIV positive patients and found a PAOD prevalence of 22.4% using ABPI as the screening tool. This study also proved a positive association between PAOD and use of protease inhibitors (OR 2.7) and also higher chance of dyslipidaemia in HIV patients treated with PI (OR 2.68).

Another important finding was the strong association of low CD4 cells with an abnormal ABPI.

Study by Gutierrez et al [90] studied the association between an abnormal ABPI and carotid artery intima-media thickness (IMT). An increased carotid intima media thickness was found to be associated with low ABPI (<0.9). Further statistical analysis demonstrated significant

differences between numbers of traditional cardiovascular risk factors in patients with low ABPI, compared to others. This study too showed significant association of low ABPI to low CD4+T lymphocyte count.

Study by Sharma et al [91] studied the prevalence of PAOD in HIV positive women (average age 39.6 years) and HIV negative women (average age 36.4 years). Low ABPI was found only in 0.9% (among the two groups of patients). Prevalence of increased ABPI was similar (7.2% vs 6.3%) among these two groups. On multivariate analysis, increased ABPI was found to be associated with smoking (OR: 2.53; 95% CI, 0.99–6.43), BMI <18.5 (OR: 11; 95% CI, 1.61–75.63) and overweight status (OR 5.4; 95% CI, 1.13–25.89). HIV positive women were also found to have a higher proportion dyslipidaemia (HDL-C  $\leq$ 35 mg/dl: 26.2% vs 5.2% and TG  $\geq$ 200 mg/dl: 13.4% vs 5.2%).

Many studies in literature used only rest ABPI with no post-exercise modifications to identify the dormant disease. And moreover, the prevalence of ABPI  $\geq$  1.3 was also high in many studies. This may probably be under estimating the magnitude of problem since an ABPI above 1.3 does not rule out arterial occlusion. It just means that, the “vessels are non-compressible/calcific”. Those studies did not probe more into the details of ABPI  $\geq$  1.3 with other screening tools (TBI or toe pressures).

Study by Van Marie et al [72] demonstrated the outcomes of HIV positive patients who were treated in a specialised vascular centre. 154 consecutive HIV positive patients attending the specialised vascular clinic of the hospital were recruited. About 59% of these patients

presented with vascular occlusive disease. Majority of patients were males (71 Vs 20).

Mean age at presentation was 44.2 years. More than 90% of the patients presented with late stage disease (Fontaine III/IV). Percentage of patients who presented with evidence of lower limb ischemia, upper limb ischemia and symptomatic carotid artery stenosis were 56.4%, 0.01% and 0.01% respectively. Traditional risk factors for PAOD were present, but the incidence was less than that in the classic atherosclerosis population.

Perioperative mortality rate was 6.95% and rate of primary amputation was 31.91%.

Secondary amputation rate was high with a poor limb salvage rate (36.1%) after femoro-popliteal bypass (considered as marker of outcome in vascular surgery as part of infra-inguinal bypass). This created more duration of hospital stay and financial burden on the patient in addition to adding a disability.

Operated patients had a relatively higher long term mortality rate approaching 20% over a mean follow-up time of 15.4 months. Poor nutritional status as assessed by albumin was found to be an important predictor of surgical outcome.

Prevalence rate of PAOD in general population is estimated to be 1% at 50 years and 3% at 60 years of age [19]. Taking into consideration this, the high prevalence obtained in the above limited studies is alarming. It also point to the fact that there could be additional risk factors which play a role in the causation of PAOD in HIV population like a low CD4 cell count.

Interestingly there are very few studies on this topic from Indian subcontinent where HIV and its associated diseases are an alarming problem. Most of the studies conducted in the west were on particular subset of patients:

The Swiss HIV cohort study [74] recruited HIV patients above 40 years (prevalence – 21%) and another study recruited pregnant HIV positive women less than 40 years (prevalence – 0.9%) [91]. Most of these studies were limited by their small sample size. There is no large scale studies conducted in this population taking into account all adult patients, especially from India.

My study aims to bring out the prevalence of this condition in HIV positive patients using cost effective, relatively sensitive tests (ABPI & post exercise ABPI+/- TBI & Toe pressure). It also aimed at assessing risk factors possibly causative in this population in Indian setting, especially looking into the details of ART use and years of therapy.

## **Chapter 4**

### **Methodology and materials**

## **Design**

A prospective cross sectional study was designed including all adult HIV positive patients ( $\geq 18$  years) during the study period

## **Duration of study**

The study was conducted from December 2012 to September 2014.

Recruitment was completed by September 2014.

## **Inclusion and exclusion criteria**

### **Inclusion criteria:**

All adult HIV positive patients ( $\geq 18$  years) presenting to the outpatient or inpatient clinics of Christian Medical College and Hospital including the ART clinic

### **Exclusion Criteria:**

All non-consenting patients

Critically ill (who cannot perform post-exercise ABPI)



**Sample size: Sample size calculated was 400**

There were limited studies in literature addressing the same research question. From those limited studies available in literature, the prevalence varied from 0.9% to 20.7%.

The study conducted by the Swiss group which took both rest and post exercise ankle brachial pressure index into consideration found a prevalence of 20.7%.

In Indian setting as well, we expected the prevalence of peripheral arterial occlusive disease to be similar. Hence it was decided to keep the expected prevalence (p) as 20%.

Precision (d) was kept at 4% to allow for a deviation of 4% on either side.

Sample size was calculated using the formula  **$4pq/d^2$**

$$\text{Sample size} = 4pq/d^2$$

$$= 4 \times 20 \times 80/4 \times 4$$

$$= 400$$

$$P = 20$$

$$q = (1-p)$$

$$d = 4$$

### **FOR IDENTIFYING POSSIBLE RISK FACTORS**

The same patients were utilized for the identification of risk factors. As we were going to have a reasonably large sample size of 400, and the number of expected outcome of peripheral arterial occlusive disease would be around one-fifth, risk factor analysis was done comfortably using multivariable logistic regression analysis.

### **Recruitment:**

### **IRB approval**

Institutional Research Board (IRB) approval was obtained for the proposed study.

### **Settings**

Adult HIV positive patients attending the outpatient and inpatient clinics of Christian Medical College and Hospital were recruited into the study.

Most of the patients were recruited from the ART (Anti-Retroviral Therapy) clinic attached to the Department of Infectious Disease Training and Research Centre (IDTRC). ART clinic was attended by about 20-30 patients per day. There are about 10 new HIV patients seen in this clinic per week. This made recruitment easy as all the patients who were attending this clinic were HIV positive patients, and there was hardly any need to look around for HIV patients from other clinics. And more over, most of these patients were being referred from other clinical departments of the hospital as well.

### **Information leaflet**

Patients were provided verbal and written (annexure: 1) information about the study. All details pertaining to the study was included in the patient information leaflet. And the leaflet was made in simple language understandable to the layman. This was prepared in four languages (English, Hindi, Tamil and Telugu) since our hospital catered to people from different parts of the country. Since my study did not involve any invasive procedure, all patients whom I interviewed were willing for the study. Probably for the same reason, they were hardly interested in reading through the entire leaflet before consenting for the study!

### **Consenting**

A written informed consent (annexure:2) was obtained from all the consenting patients. Consent forms were also made in all four languages described above. Consent form included all the details pertaining to an ideal consent form.

### **Data collection**

Data was collected using a preformed proforma (annexure:3).

The proforma was divided into many parts.

First part included demographic details of the patient. It also included hospital number of the patient and a study code no against all these hospital numbers so as to conceal the identity of the patient. Patients were explained that their identity will be concealed. And this was of greater concern for most of the patients whom I recruited owing to the nature and stigma of the disease they are living with.

Second part included the Edinburgh Claudication Questionnaire (as described elsewhere).

This questionnaire was used initially to categorize consented patients into – Symptomatic and asymptomatic. Only those patients who give “YES” to all questions in the questionnaire will be considered as having true claudication.

Irrespective of being having true claudication, all patients will undergo ABPI with toe pressures since it is shown in the Swiss study and others that prevalence of asymptomatic peripheral arterial occlusive disease is higher in this particular group (HIV patients). These cases are the ones whom I was expecting to pick up by the post-exercise regime.

Third part included traditional risk factor assessment.

Fourth part includes the treatment (HAART) details.

Treatment information was obtained from the ART notebook maintained by all these patients.

Information with respect to the date of diagnosis, enrolment for ART, drug regime, recent CD4 count, reason for drug change were all could be obtained from this books alone.

Fifth part included the clinical examination including palpation of all peripheral pulses and appropriate documentation.

Sixth part includes the entry of available lab parameters of significance to my study.

Last part included the measurement of ABPI and Toe pressure and its documentation.

Dyslipidaemia was diagnosed based on a history of dyslipidaemia, history of lipid lowering drug intake, or defined based on Third Report of the National Cholesterol Education Program (NCEP) as triglyceride  $\geq 150$ , LDL cholesterol  $\geq 130$ , total cholesterol  $\geq 200$  or HDL cholesterol  $<40$  mg/dL[92]

Hypertension was diagnosed based on history of HTN, history of antihypertensive intake or as defined by the JNC7 guidelines: In people aged 18 years or older hypertension is defined as a systolic and/or a diastolic blood pressure measurement consistently higher than an accepted normal value (currently 139 mmHg systolic, 89 mmHg diastolic) [93]

Diabetes mellitus was diagnosed based on a history of known DM, history of anti-diabetic medications, or WHO criteria by demonstrating any one of the following: fasting plasma glucose level  $\geq 126$  mg/dl and/or 2 hours post prandial plasma glucose  $\geq 200$  mg/dL [94]

The collected data was compiled and was analysed for distribution of disease at the end of study. Risk factor were documented as “present” if the answer to the following questions were given as “YES”. A “NO” response will be marked as “absent” risk factor.

- Do you smoke / ever smoked? How often?
- Do you use tobacco in any other form? How often?
- Do you drink alcohol on a regular basis? How often?
- Do you have a past history of vascular events?
- Do you have a family history of any of the above events?
- Are you a diagnosed case of DM? History of anti-diabetic medications?
- Are you a diagnosed case of HTN? History of anti hypertensives?
- Are you a diagnosed case of dyslipidaemia? History of lipid lowering agent intake?

All patients who were found to have evidence of peripheral arterial occlusive disease were informed regarding the same.

All patients were explained regarding the need for further evaluations and treatment.

They were explained regarding the limitation of my study in providing further evaluations and treatment.

All patients were referred to the Department of Vascular Surgery unit of our hospital for further evaluations and management if necessary. But majority of them had not turned up to the clinic so far.

Health education with respect to the peripheral arterial occlusive disease and life style and risk factor modifications were explained to them.

A total of 403 such patients were recruited wherein the calculated sample size was 400. Originally planned for 400, at the end of final data entry it was found that 403 patients were recruited. But owing to the benefits of adding on those patients and also to avoid bias, they were not excluded. These three patients were included for the final analysis as well.

All patients had to be recruited by myself and all patients required ABPI to be measured by me. This was made a compulsory in the study design so as to avoid the inter observer variability. For the same reason, it was not possible to recruit all consecutive patients due to the time constraints of a post graduate student.

#### **Measurement of ABPI and Toe pressure**

Ankle brachial pressure index was measured using a hand held Doppler machine and standard blood pressure cuff attached to a sphygmomanometer.

All patients were required to rest in supine position for 5 minutes

Rest ABPI was measured in the standard way as described in literature.

All patients made to walk for 10 minutes under supervision

Post exercise ABPI was measured in a similar manner.

Bilateral ABPI was calculated and entered in the proforma.

All patients whose ABPI was  $>1.1$  (after rounding off) were sent to the Vascular lab attached to the Department of Vascular Surgery of our hospital for bilateral toe pressure measurement.

Toe pressures were measured in the standard way and entered in the proforma.

The diagnosis of peripheral arterial occlusive disease (primary outcome) was based on the

**AHA (American Heart Association) guidelines (25):**

Any ABPI (Ankle Brachial Pressure Index)  $<0.90$  will be taken as significant.

In those patients where there is evidence of calcific, non-compressible vessels (Ankle brachial pressure index  $>1.1$  (like chronic kidney disease and diabetes mellitus), following guidelines were used for diagnosis of PAOD.

- Toe pressures (TP)  $<50$  mm Hg and/or
- Toe brachial index (TBI)  $<0.7$

These are the standard cut off used worldwide and even in our institution.

A post exercise reduction in the ABPI value was considered significant if;

- The value fall to abnormal, i.e  $<0.9$  and/or
- $>25\%$  reduction from the baseline value





Above figure shows the basic instruments needed for measurement of ankle brachial index which includes:

- Hand held Doppler machine
- Blood pressure cuff with sphygmomanometer
- Lubricant jelly.

These instruments can be portable and hence the measurement of ABPI becomes easy in all settings.



This picture shows ankle pressure being measured in the right posterior tibial artery. Note the supine position of the patient and the place at which the blood pressure cuff is tied.



This picture shows ankle pressure being measured at the left dorsalis pedis artery. Again note the position of patient and position of blood pressure cuff.





Toe pressure cuff being attached to the right big toe for measurement



Toe pressure being measured in the right big toe. Note the wave form in the screen which depicts presence of active blood flow

### **Data entry**

Information from the proforma was entered in Microsoft excel sheet for future analysis and interpretation. This excel sheet with the hospital numbers were made available only to the primary investigator, co-investigators and the guides. Other persons who had helped in the preparation of final paper were given only the study code numbers.

### **Maintenance of data and confidentiality preservation**

HIV positive status of the patient was kept confidential. All study related records were in the sole custody of the Principal Investigator. Completed consent forms and questionnaires were locked in cupboards. All digital data were stored in password-protected computer file.

To further protect the identity of the participants, each person participating in

Each patient was assigned a study code number at the top of their consent form, which was used whenever possible instead of that person's personal identity details. This code number was used for communications with a third party excluding the guide and co-investigators. This way the third parties were unaware of the patient details.

### **Outcomes measured**

#### **Primary Outcome:**

To measure the prevalence of peripheral arterial occlusive disease (PAOD) in adult HIV positive ( $\geq 18$  years)

#### **Secondary Outcome/s:**

Identification of risk factors in the causation of PAOD in this population

## **Statistical Analyses**

- Data entry was done using Microsoft Excel.
- Descriptive analysis of the study population was done.
- Prevalence/frequency distribution of disease in each subset group (Eg: Diabetics, tobacco users, CD4 <300 HIV patients) was calculated separately.
- Risk factors and lab parameters under study were initially examined using a univariate analysis with chi-square test.
- Selection of risk factors was based on both clinical and/or statistical usefulness.
- Multivariate logistic regression analysis was performed to identify independent factors that are associated with risk of developing PAOD in this population.
- All analysis was done using SPSS statistical software.

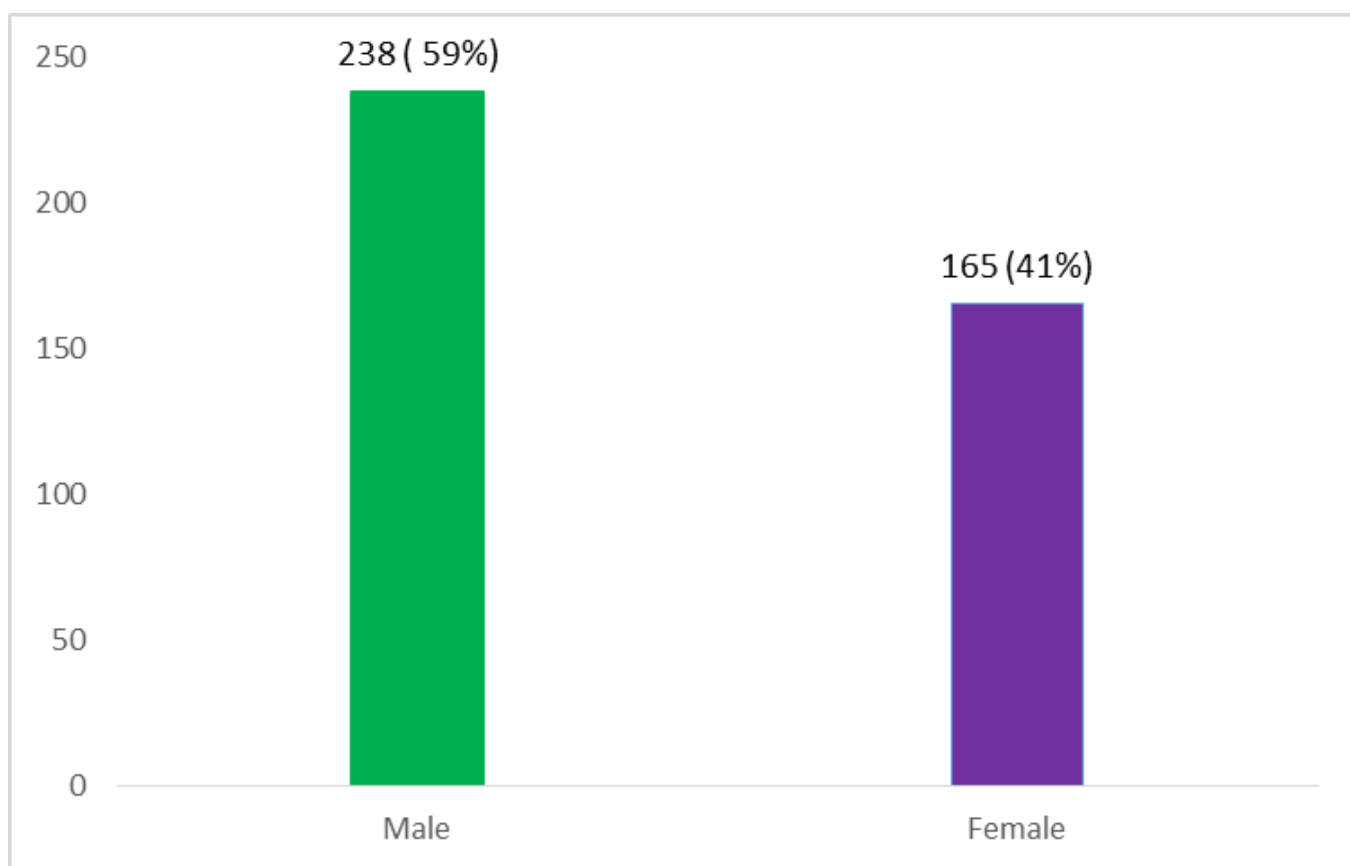
## **Chapter 5**

### **Results**

A total of 403 patients were recruited into the study over the proposed time period.

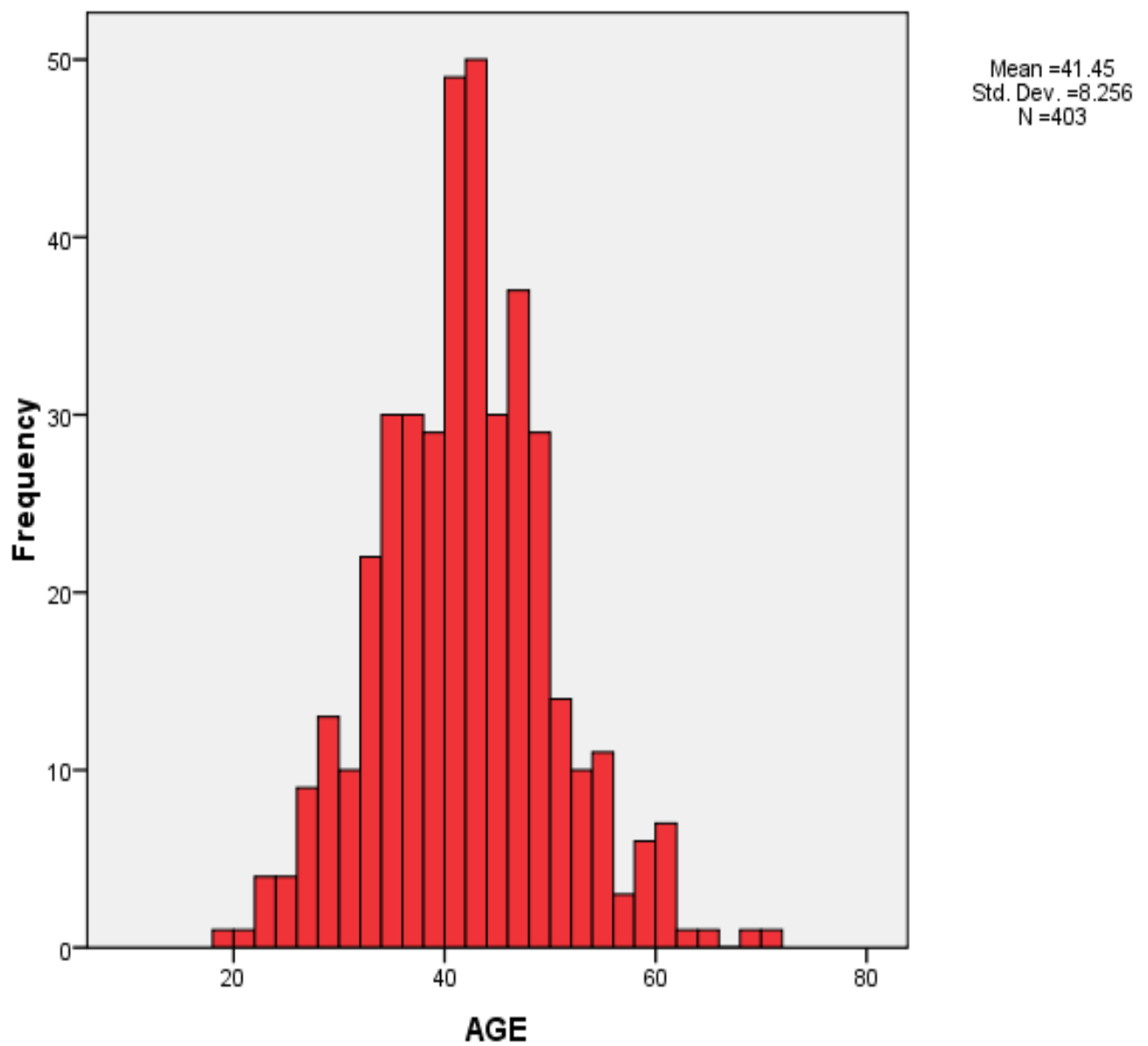
## 1. Demography – results

### Sex



Out of 403, 238 patients (59.1%) were males and 165 (40.9%) were females.

### Age (years)

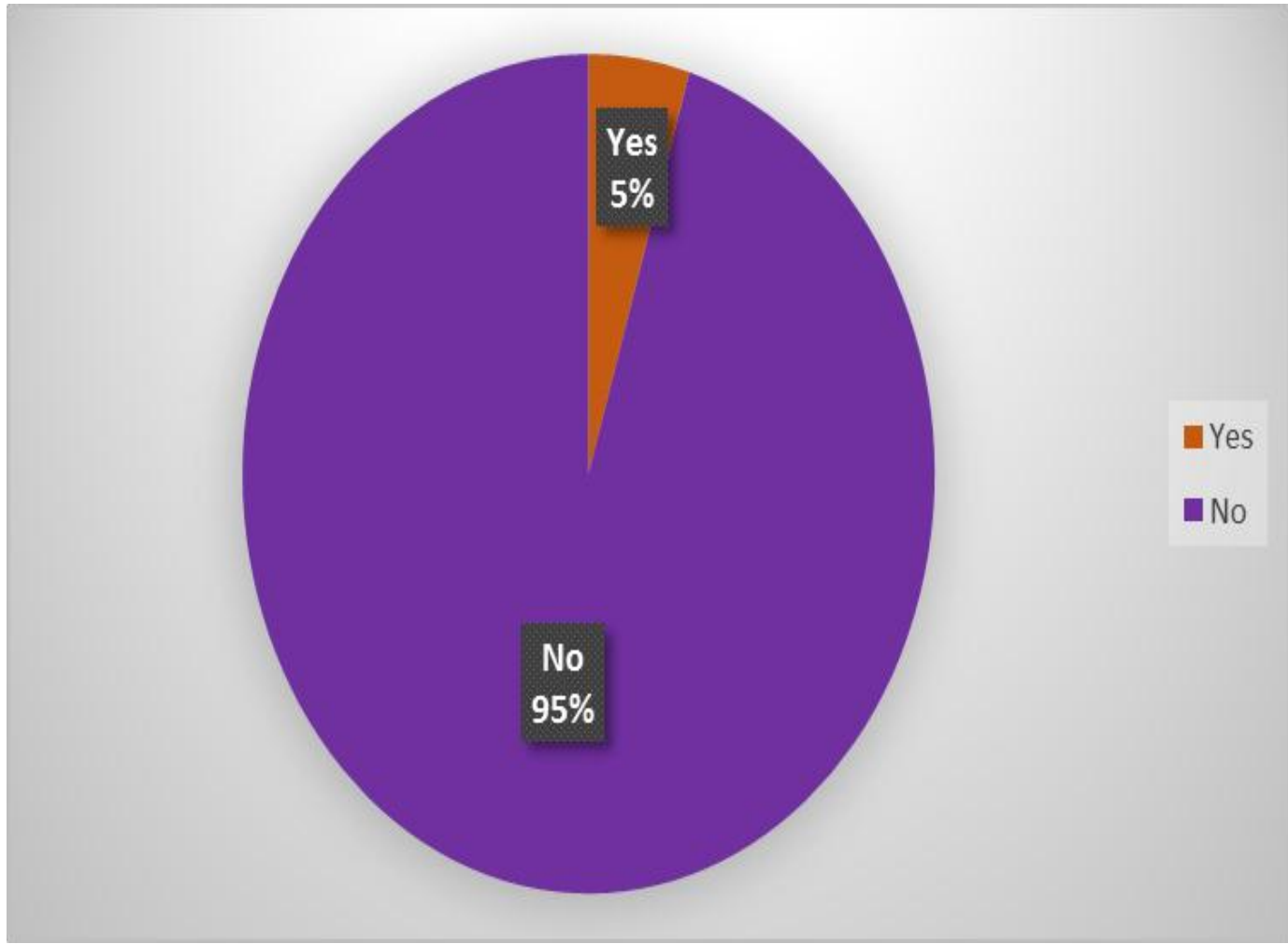


- Average age of the study population was 41.45 years.
- Majority of patients were in 30-50 age groups as depicted in the histogram.



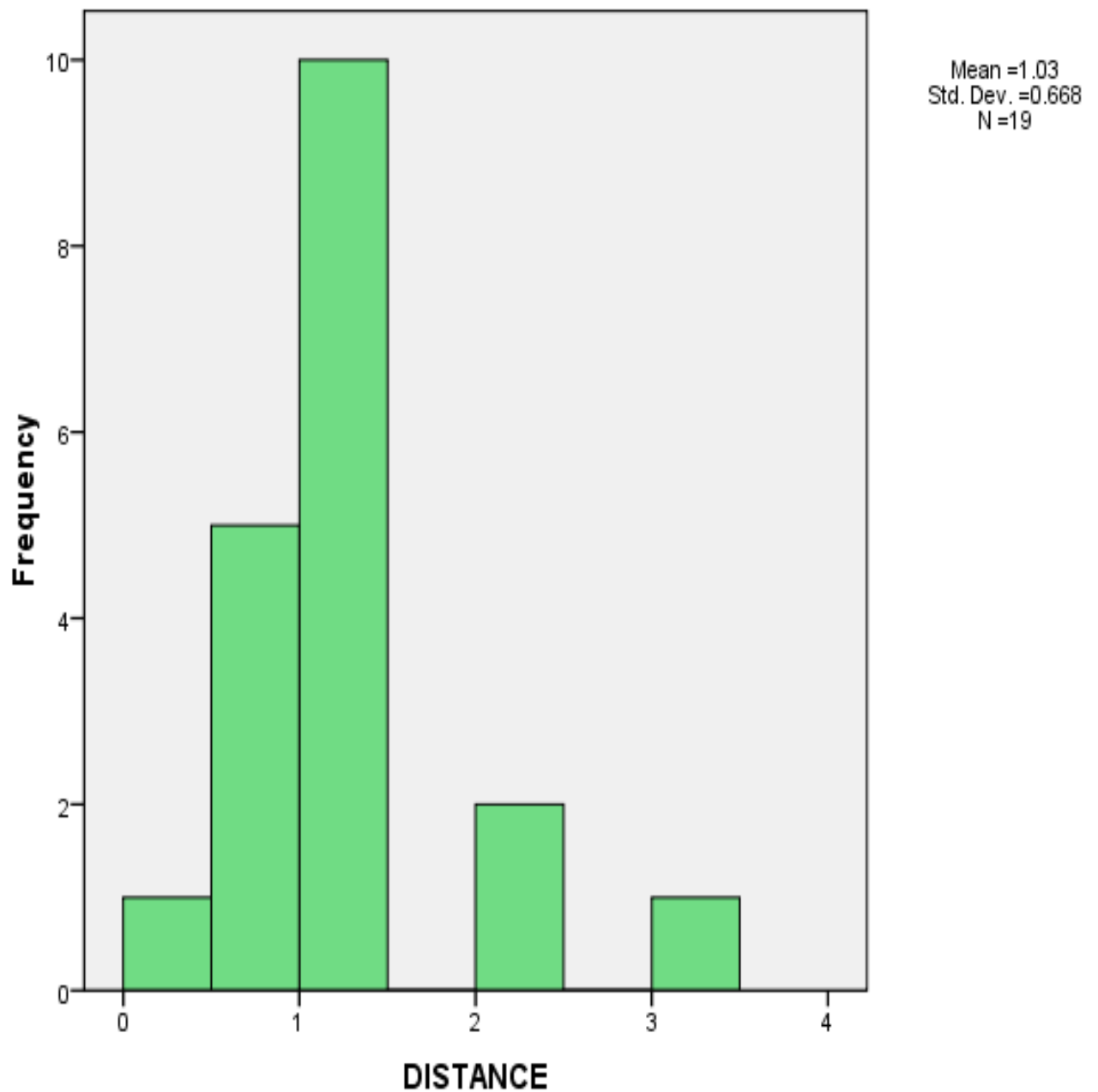
## 2. Symptomatology – results

### Claudication



19 patients (5%) reported claudication as per the Edinburgh Claudication Questionnaire.

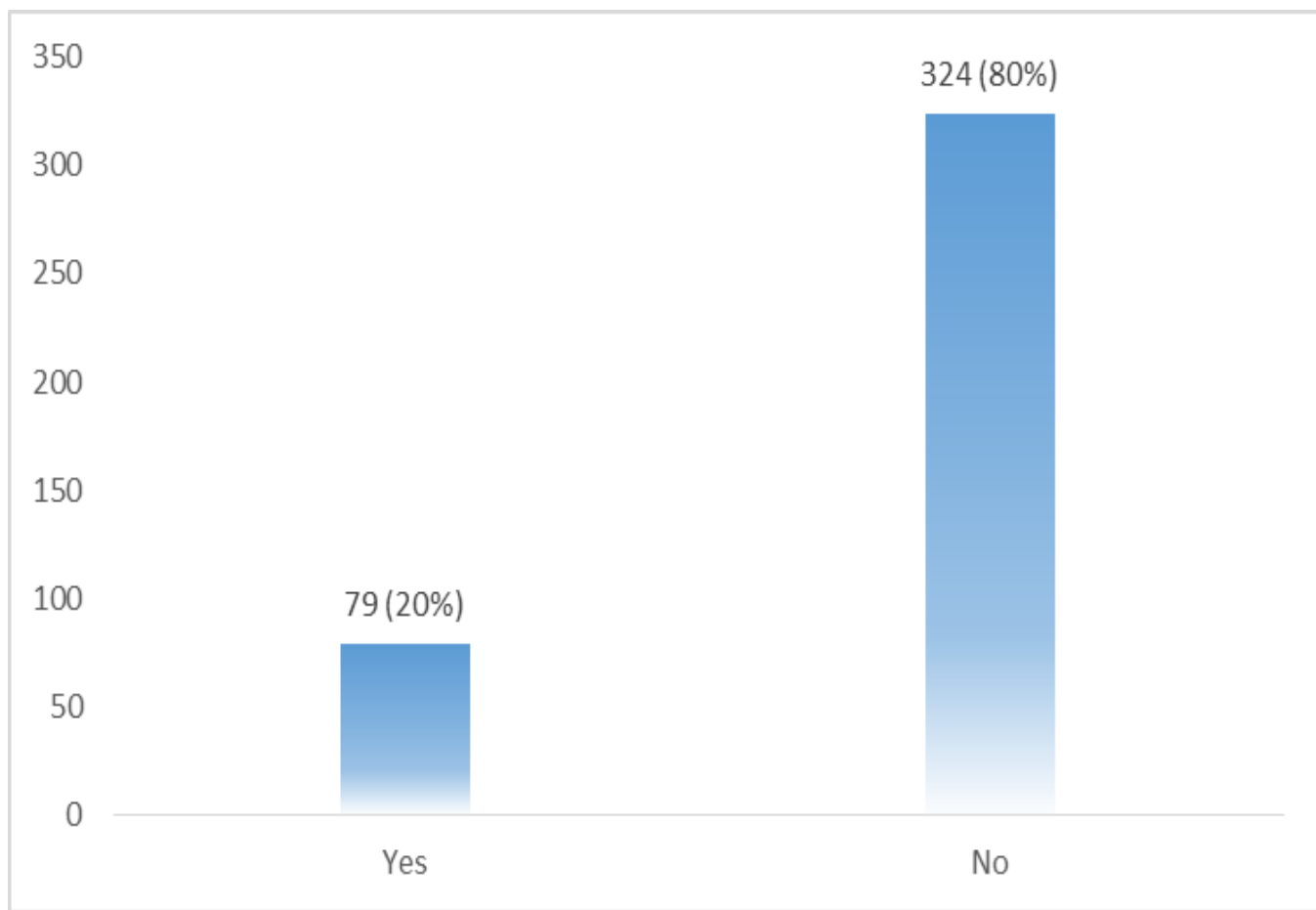
**Mean claudication distance (Kilometres)**



- Mean claudication distance by the claudicants was 1.03 kilometres.
- No patient reported rest pain or features of tissue loss (ulcers or gangrene) especially among the claudicants.

### 3. Traditional risk factors- results

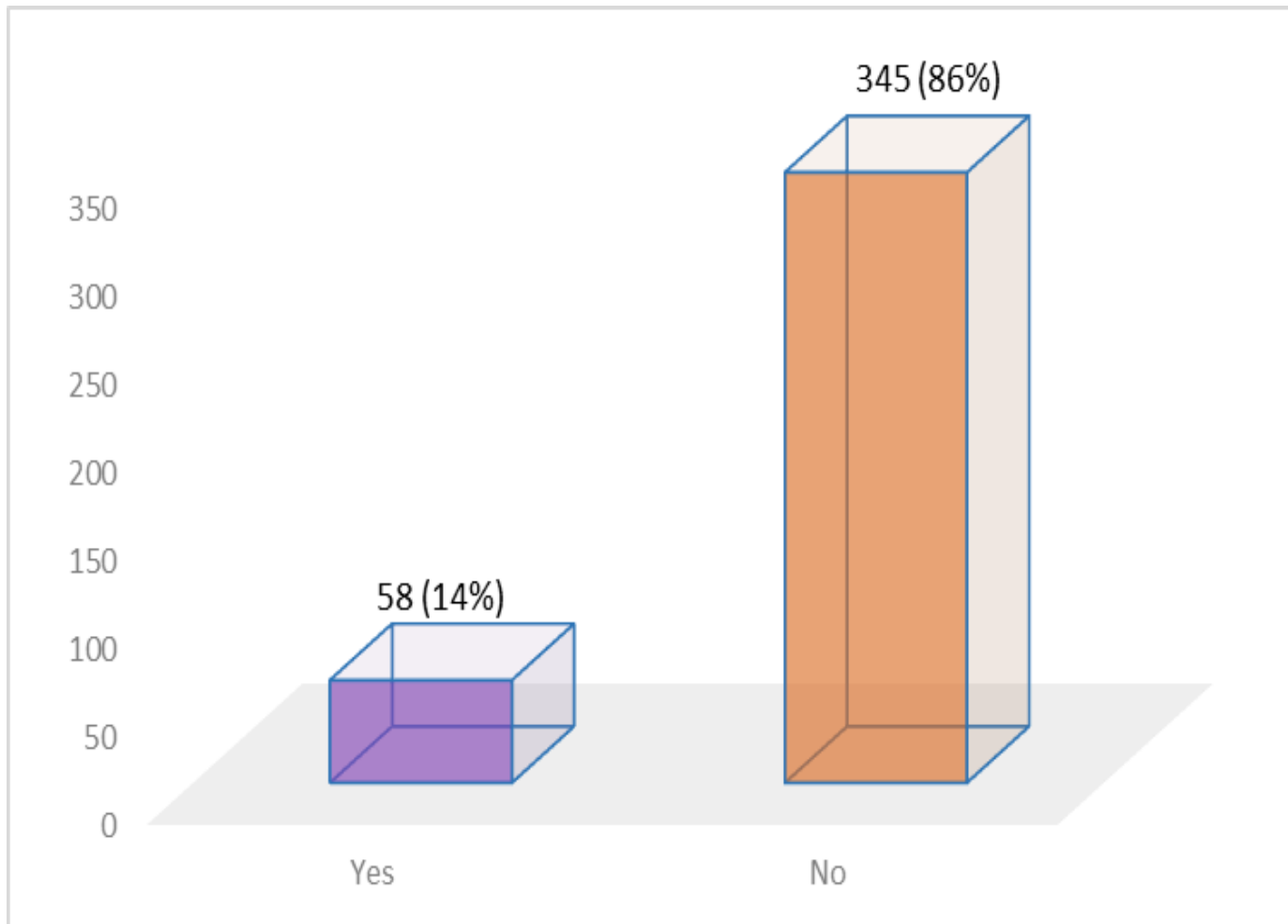
#### Tobacco



- 79 (19.6%) patients used tobacco in some form.
- Predominant form of tobacco use was smoking.

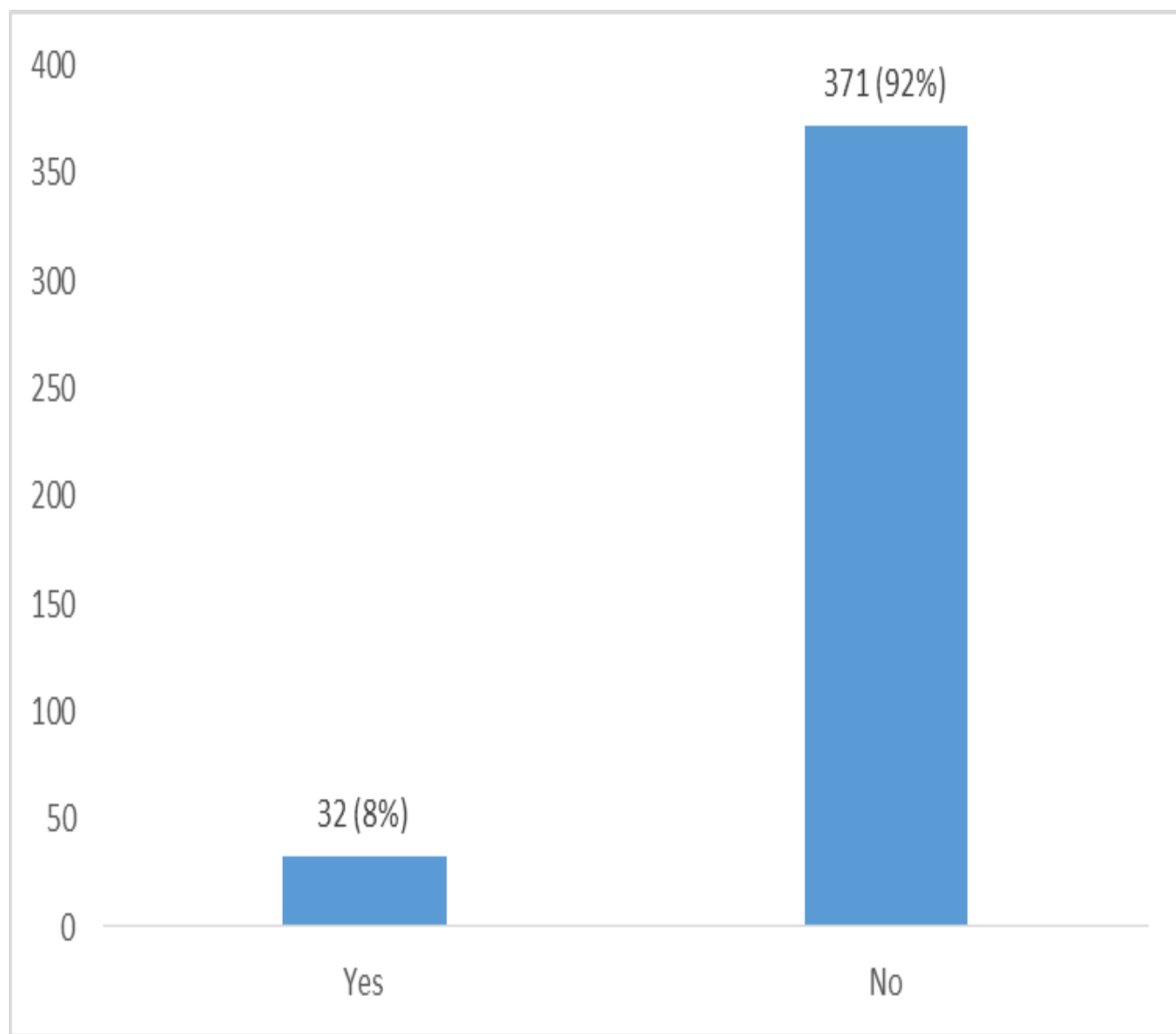
## Alcohol

(History of this was obtained as to see for any relation in this particular population with causation of PAOD – it is not a traditional risk factor)



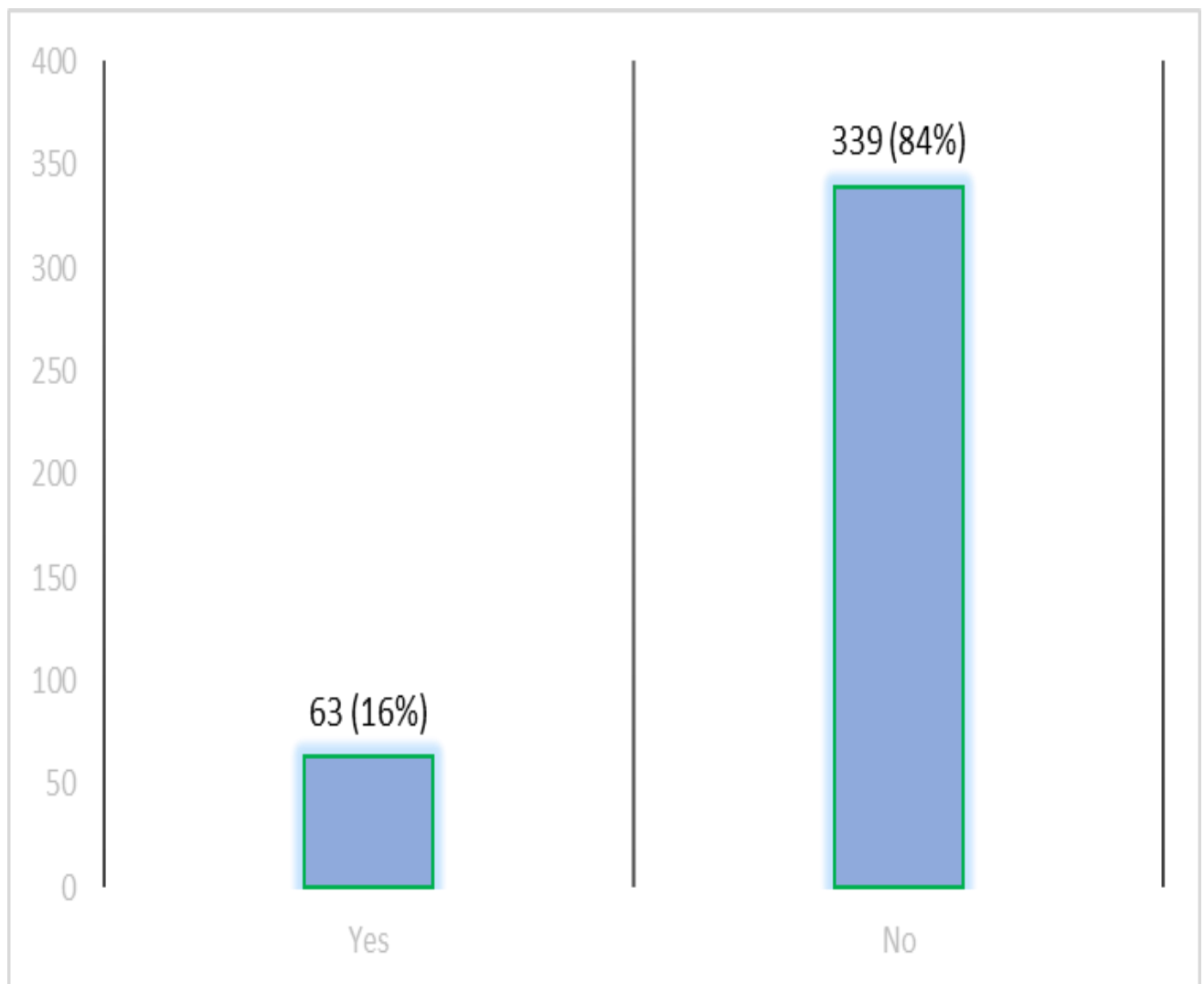
- Alcohol was used by 58 (14.4%) patients.
- 57 were males and 1 was female.

### **Diabetes mellitus**



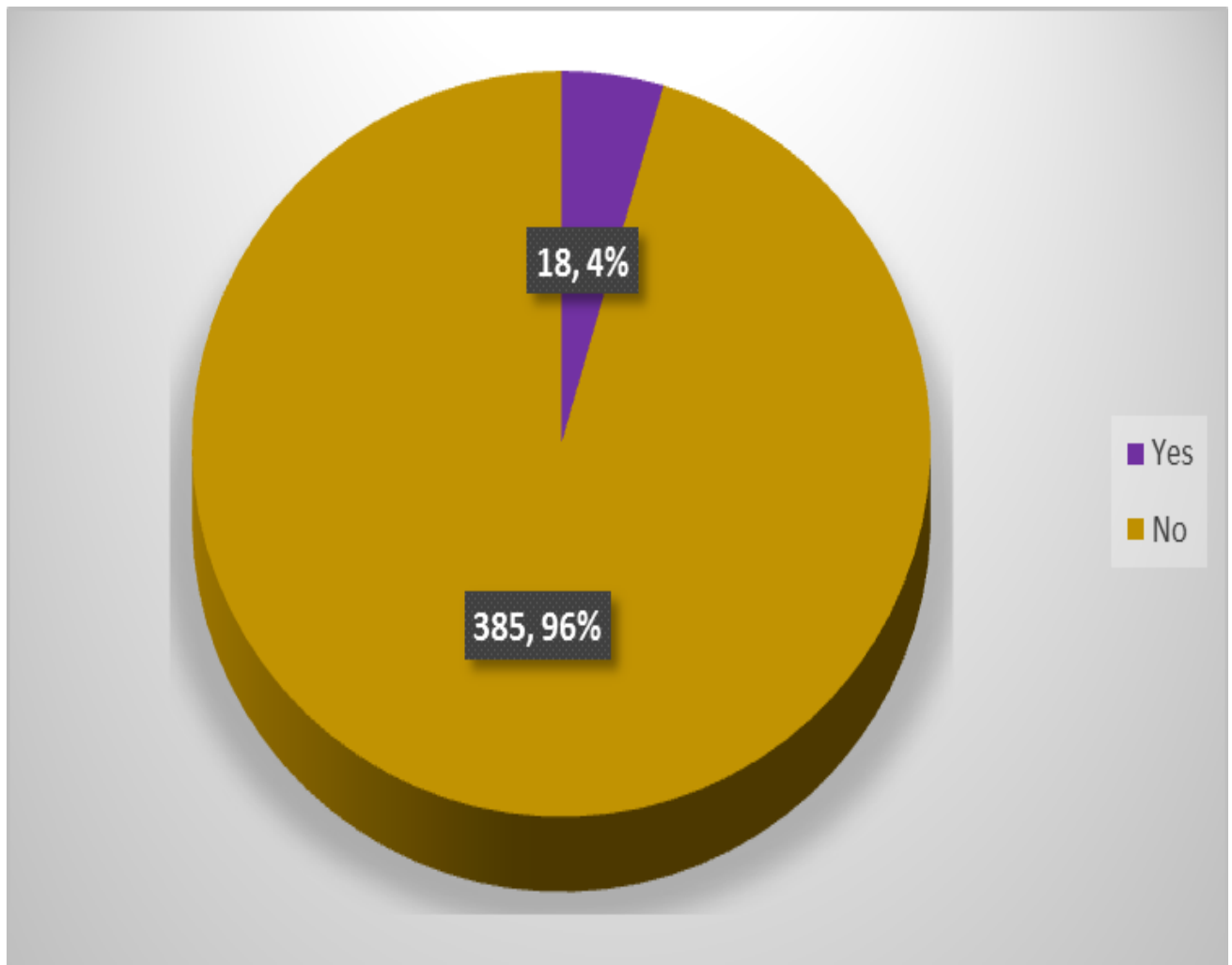
32 patients (7.9%) were diabetic and 371 (92.1%) were non-diabetic.

## Hypertension



- 63 patients (15.63%) were hypertensive and 340 patients (84.37%) were not diagnosed with hypertension.
- Majority of the hypertensive patients in this population was irregular on treatment.

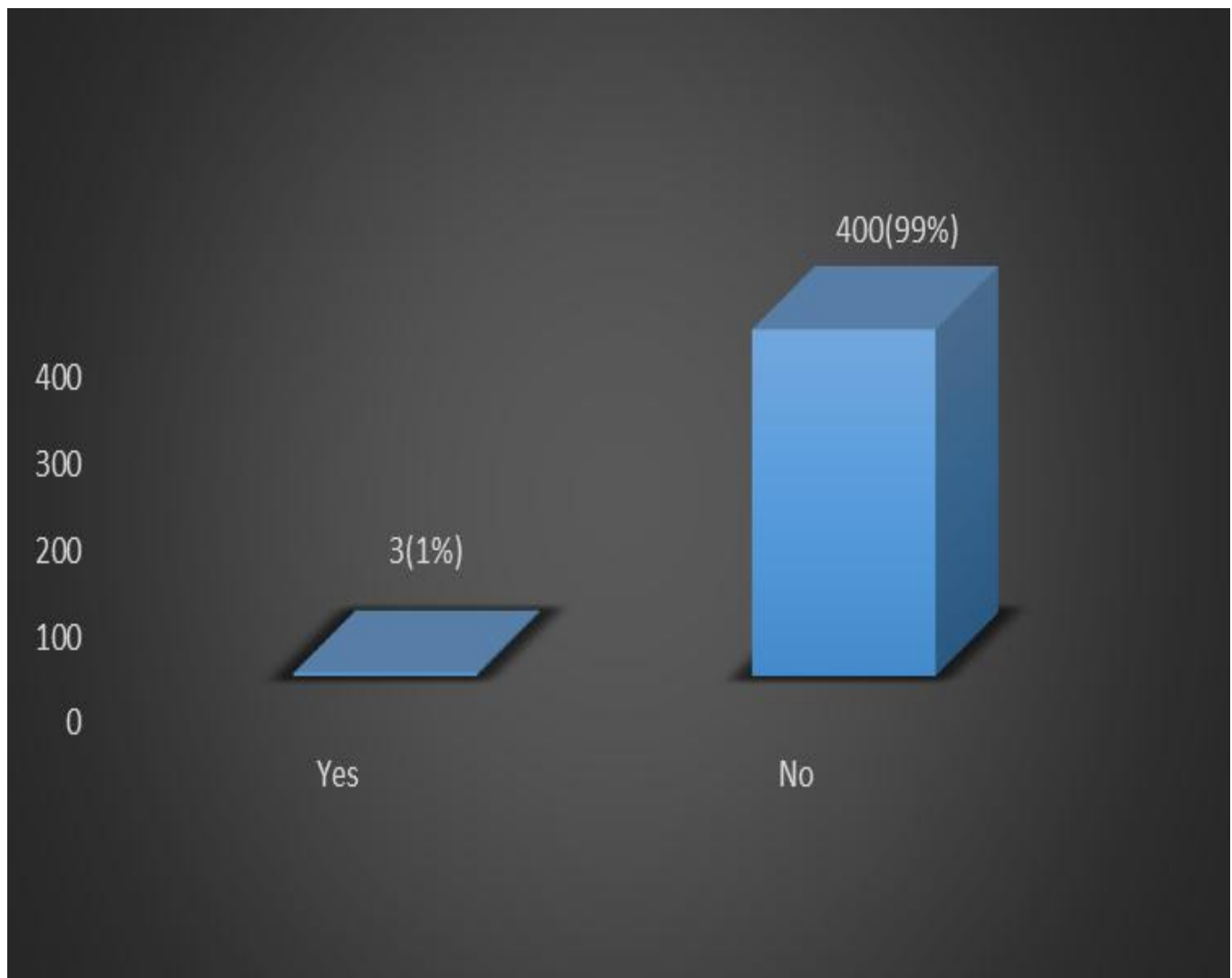
## Dyslipidaemia



- 18 patients (4.5%) were diagnosed with dyslipidaemia and 385 patients (95.5%) were not diagnosed with dyslipidaemia.
- Majority of patients who were diagnosed with dyslipidaemia were on life style modifications rather than medications.

Ischemic heart disease/Acute coronary syndrome/ angina/coronary artery disease

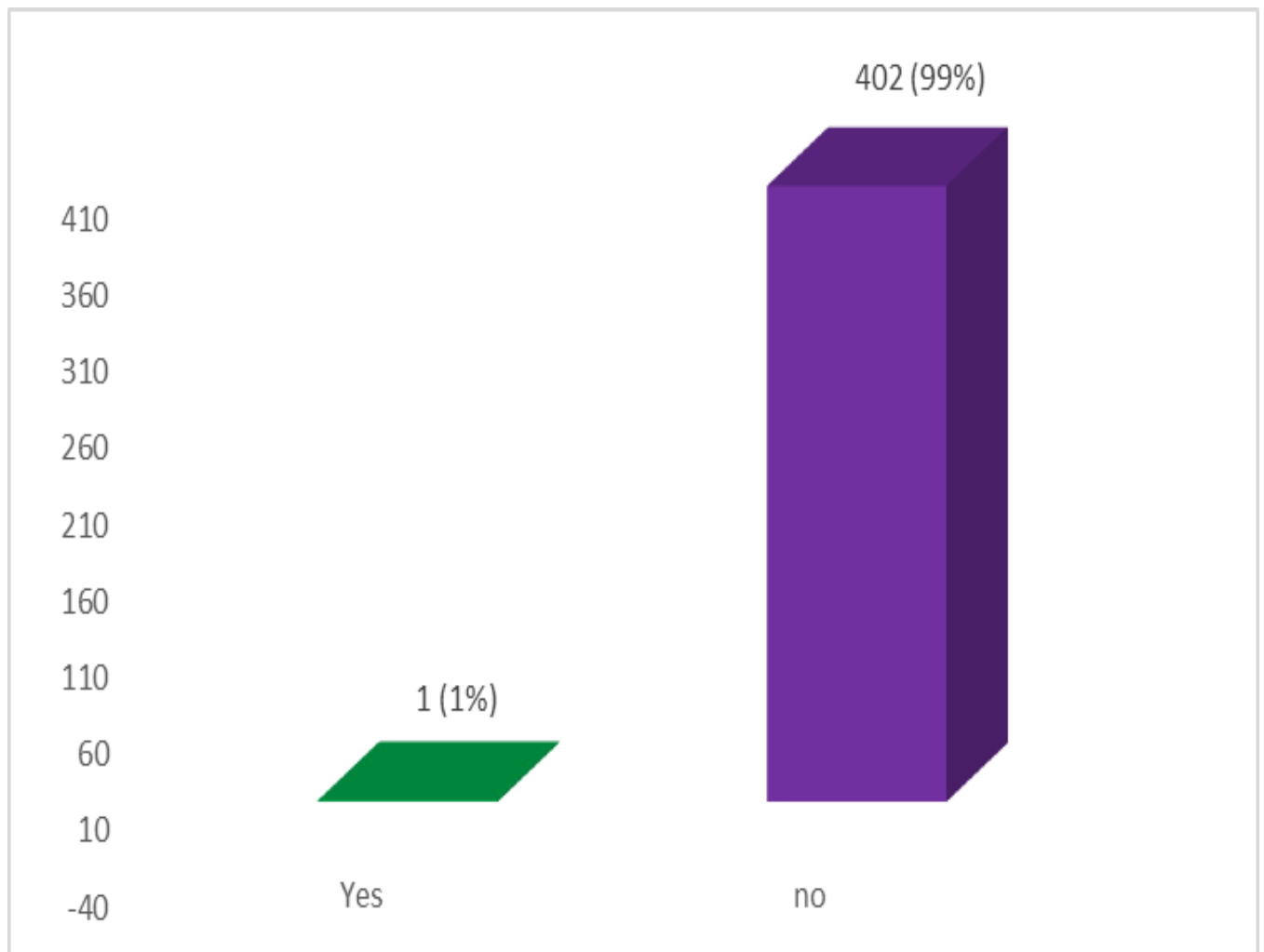
(IHD/ACS/CAD)



3 patients (0.7%) had prior history suggestive of ischemic heart disease/acute coronary syndrome/coronary artery disease/history suggestive of coronary angina.

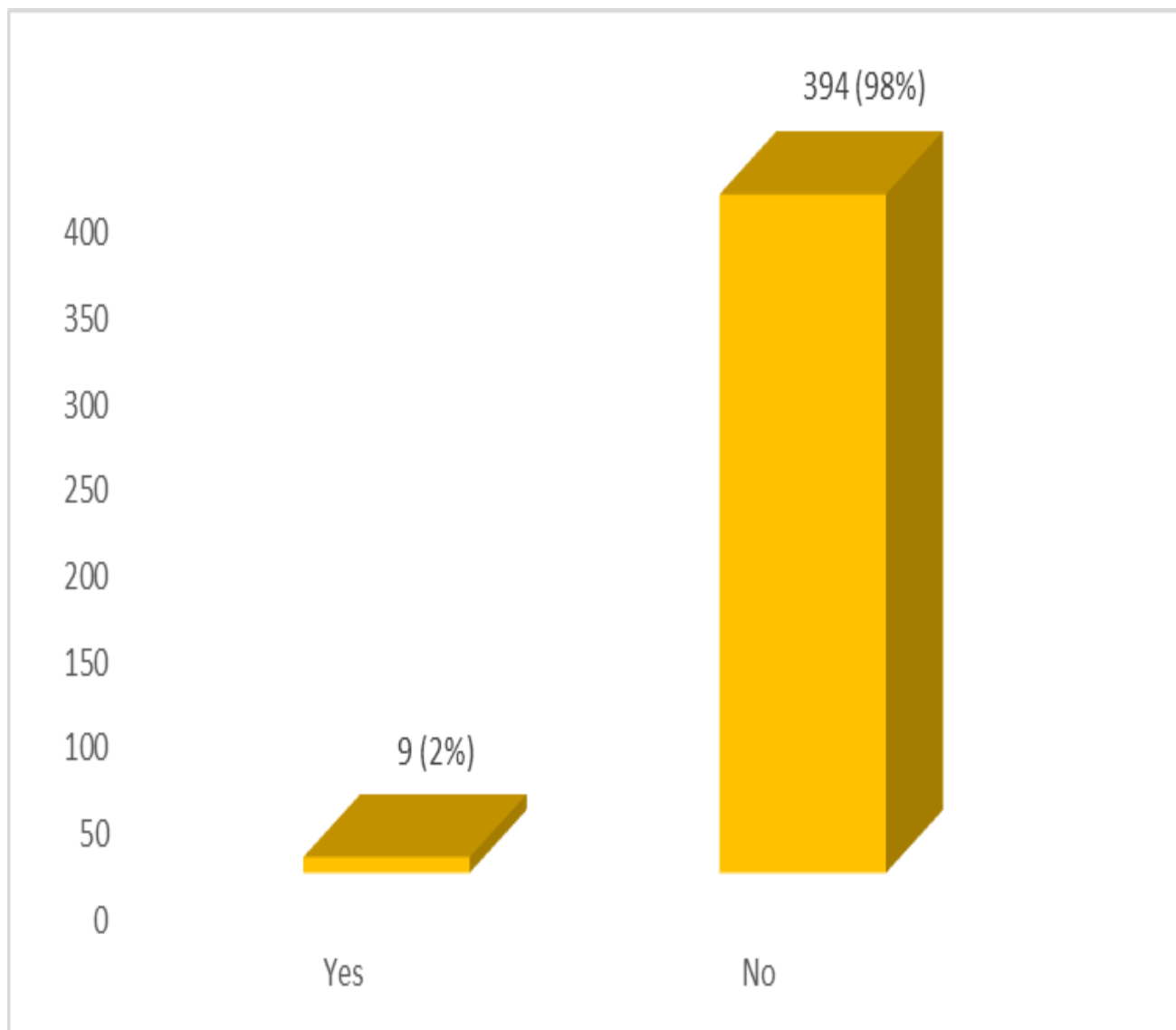


**Cerebrovascular accidents/transient ischemic attacks (CVA/TIA)**



1 patient (0.2%) had history of prior stroke from which the patient had recovered completely.

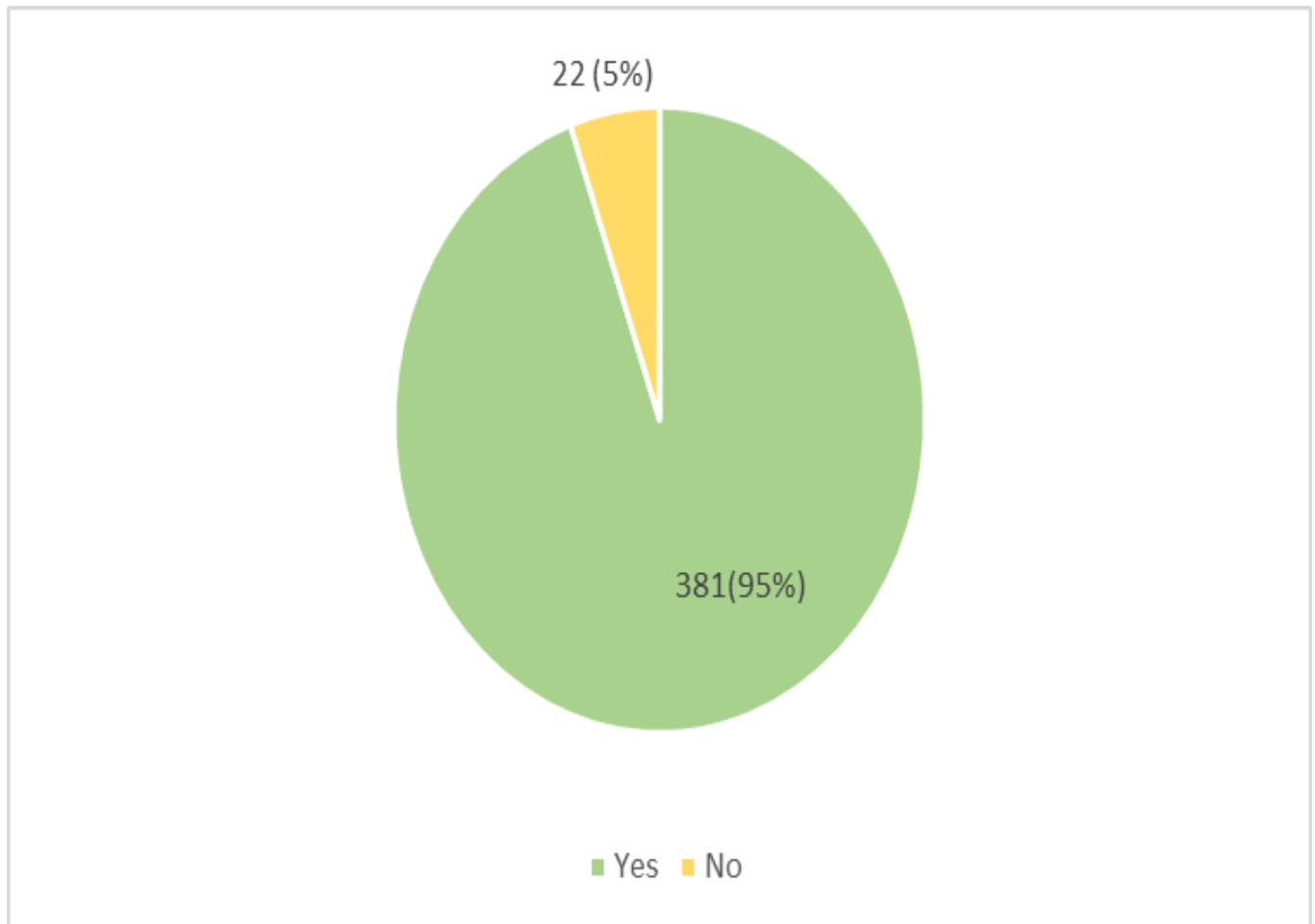
**Family history of vascular events/vascular disease**



9 patients (2.2%) had history suggestive of some vascular disease in the family.

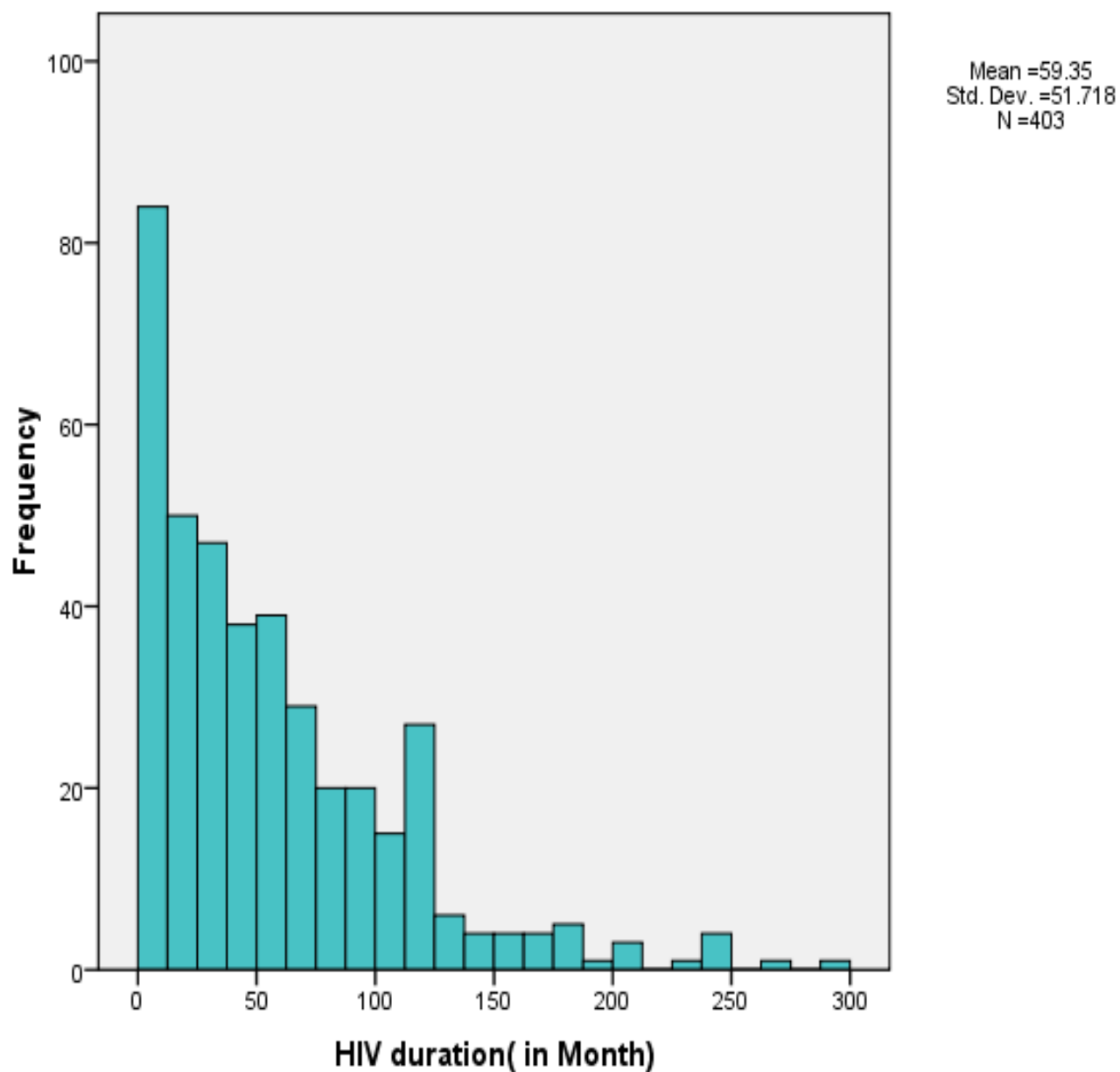
### 3. Treatment details – Results

#### ART patients



- Among 403 patients, 381 patients (95%) were currently on ART and 22 (5%) were not yet initiated on ART.
- These patients who were on ART, all were regular on treatment currently.
- Among those who were not on ART, the immune status as assessed by CD4 count was good.

**Duration of HIV (months)**



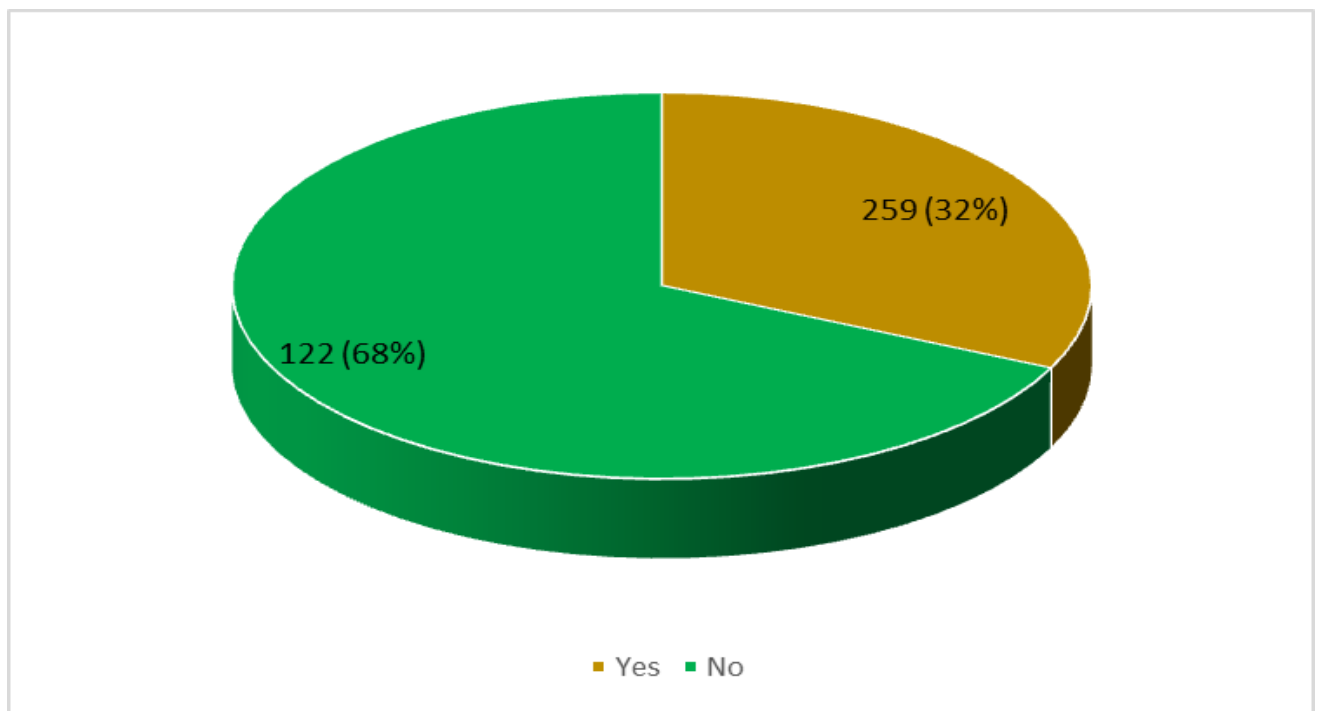
Mean duration since HIV was diagnosed was 59.35 months

### **Drug regime**

Most of the patients were on ZLN (Zidovudine, Lamivudine and Nevirapine) combination therapy.

But recently there was a change on the regime to TLN (Tenofovir, Lamivudine and Nevirapine) or TLE (Tenofovir, Lamivudine and Efavirenz) owing to a higher incidence of Zidovudine induced anemia.

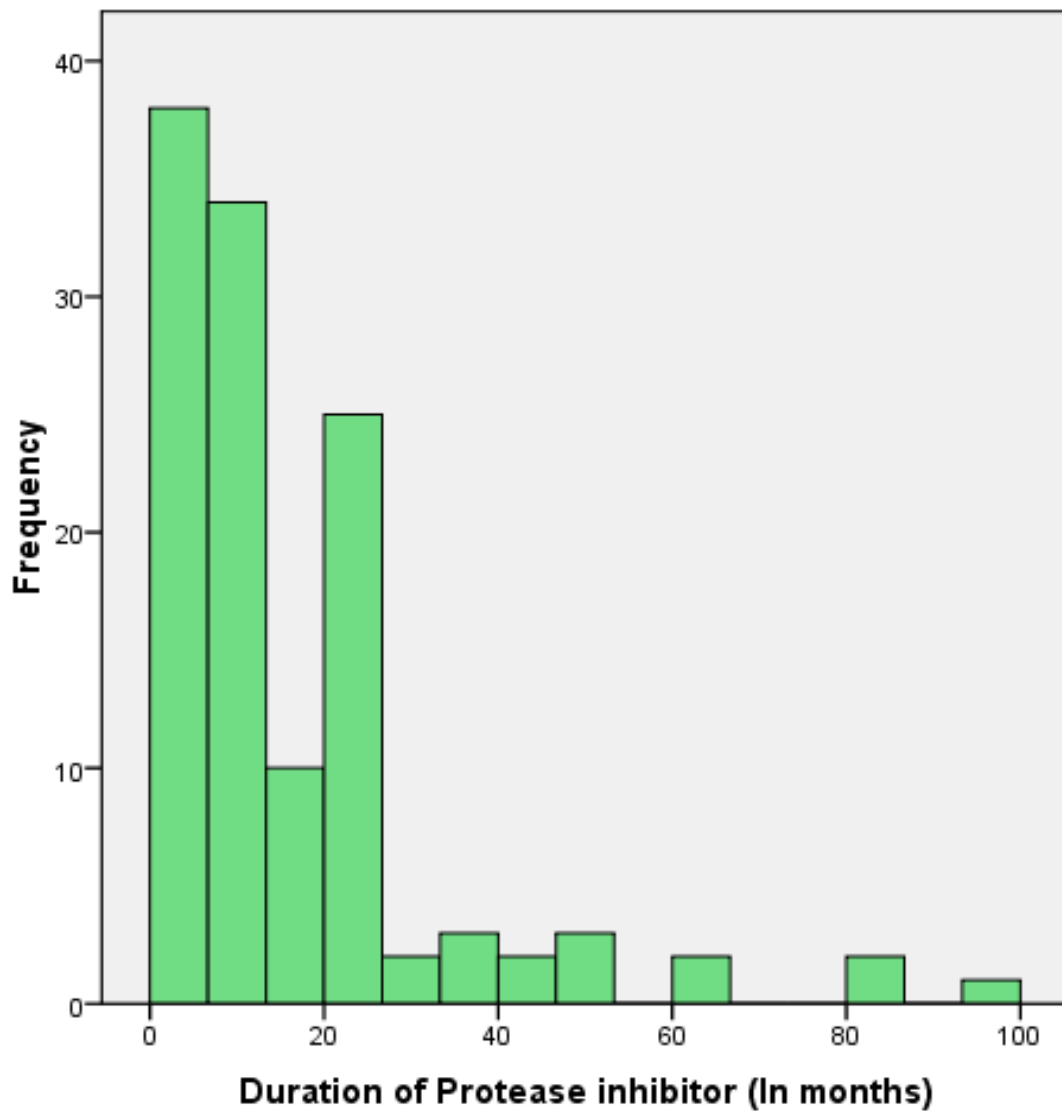
### **Use of protease inhibitors (PIs)**



Among the 381 patients who were on ART:

- 122 patients were on one of the protease inhibitors at least or had history of using one of the protease inhibitors in the past.
- 259 patients never had history of protease inhibitor use.

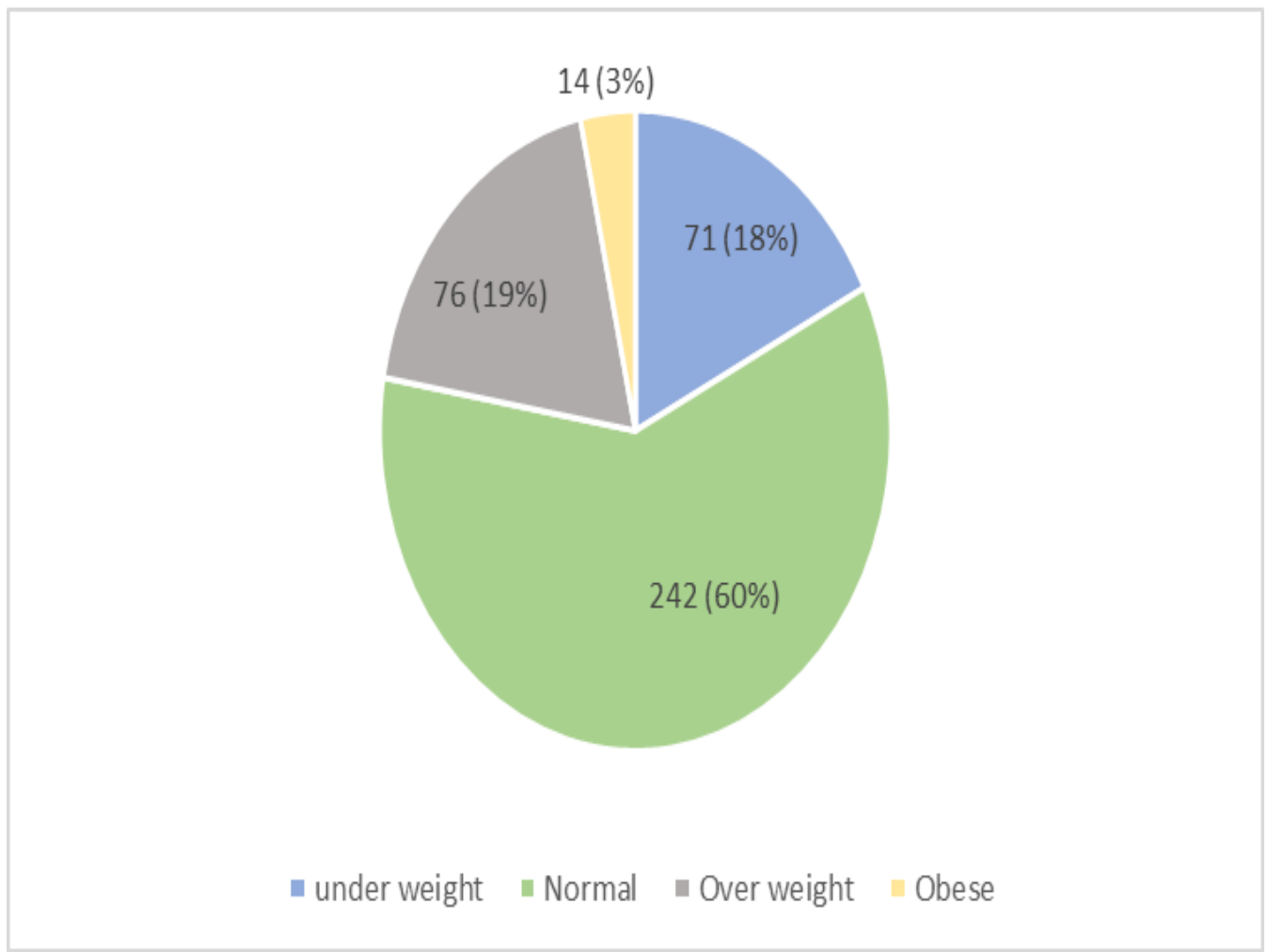
**Duration of protease inhibitor (PIs) use (months)**



- Mean duration of protease inhibitor use was 16.57 months.
- Majority of patients had history of using protease inhibitors for less than 30 months.

This could explain the recent trend of changing to a drug regime based on one of the protease inhibitor.

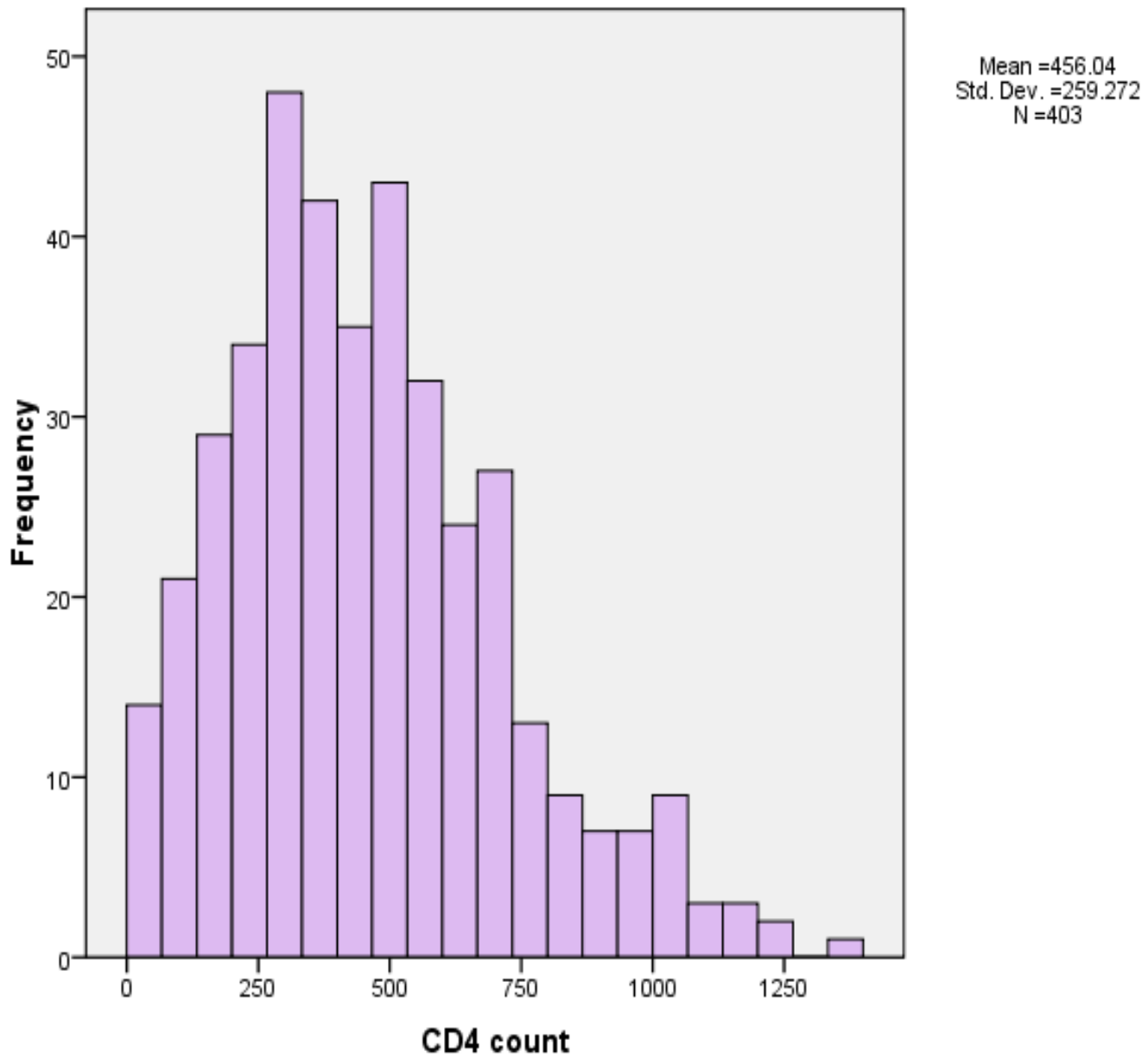
#### 4. Body mass index (BMI)



Among 403 patients, majority of patients fell into the normal category and there was almost equal percentage of patients who were overweight or underweight.

This also point towards a better nutritional status of these patients in spite of being having an immune suppressive disease.

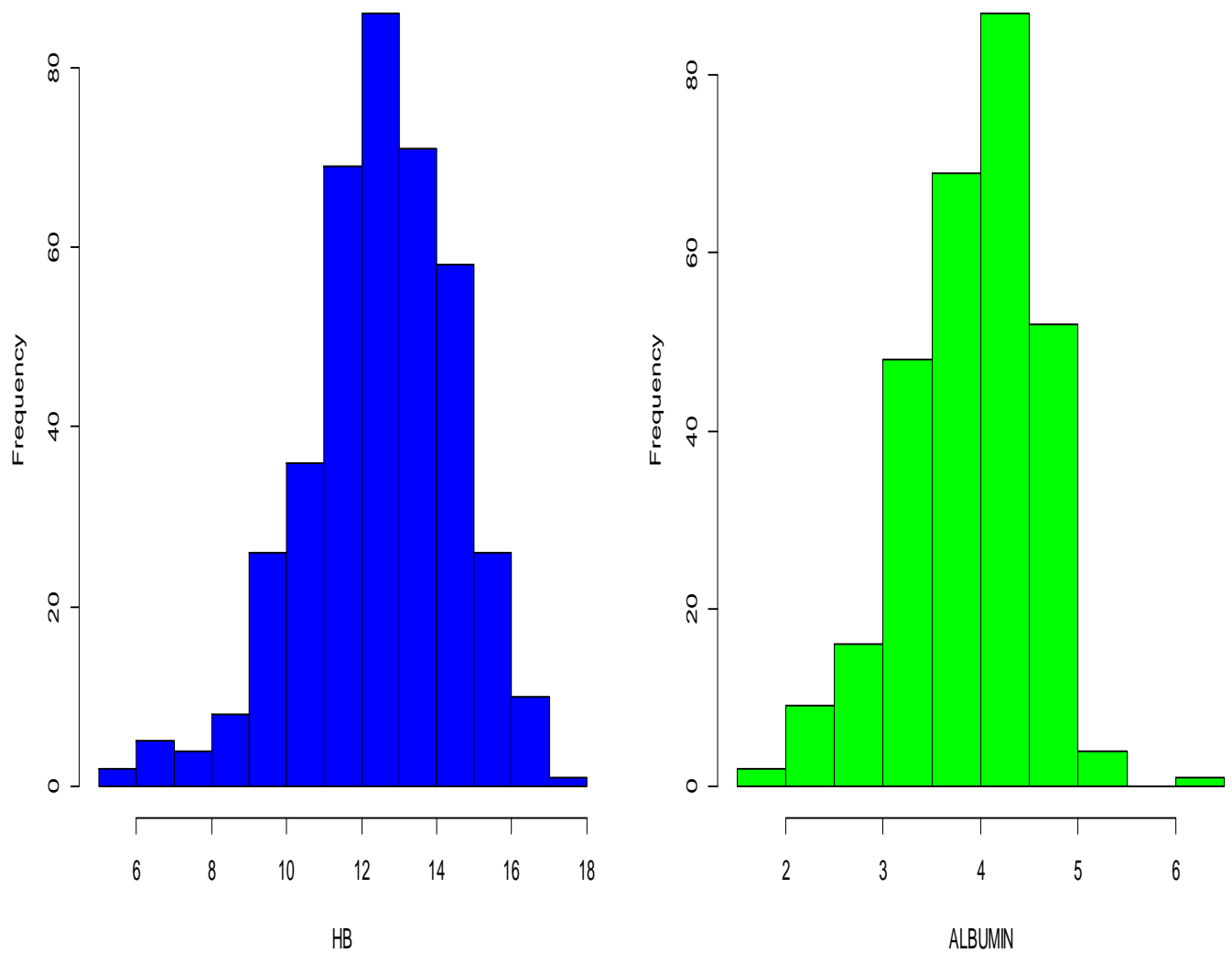
## 5. CD4 count



- Mean CD4 count was 456.04.
- This reflected a good immune system in majority of patients, probably related to regular HAART therapy with suppressed viral load.



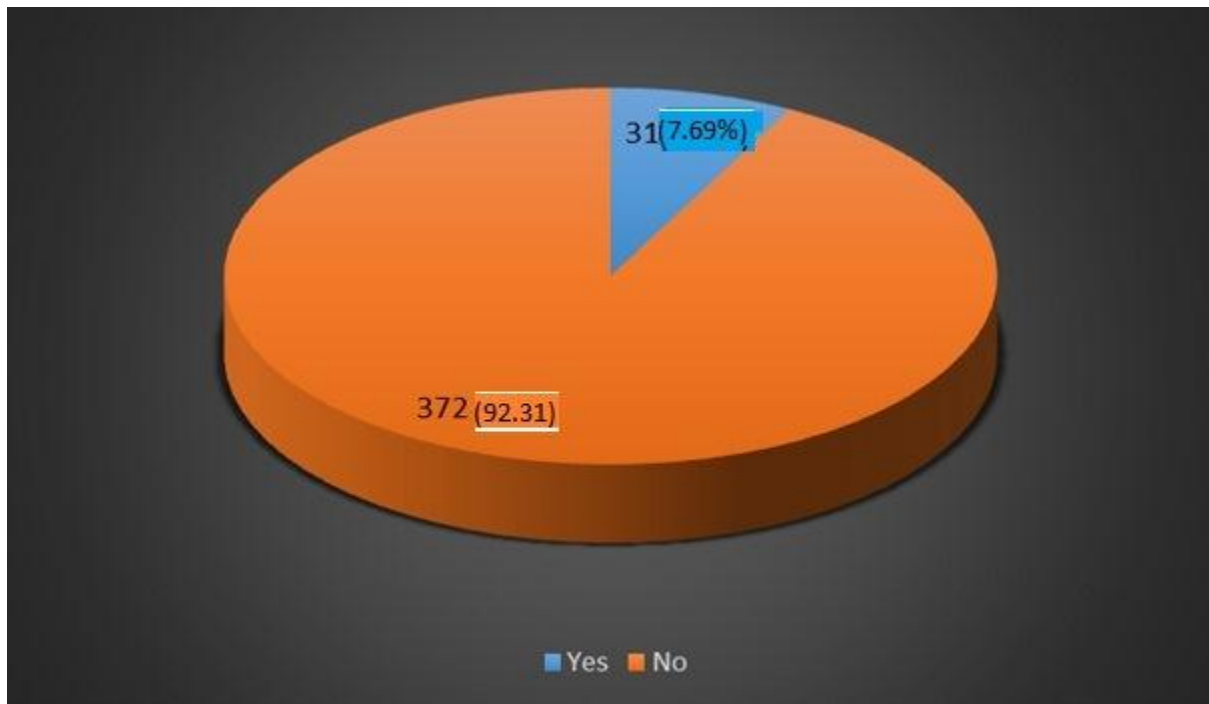
## 6. Haemoglobin (gm %) and Albumin (gm%) levels



- Mean haemoglobin was 12.52 gm%.
- Mean albumin was 3.97 gm%.

These two factors again reflected the good nutritional status of this group of patients in spite of having acquired an immunosuppressive infection.

### Prevalence of peripheral arterial occlusive disease (PAOD)



- Among 403 patients, peripheral arterial occlusive disease (PAOD) was identified in 31 patients using ABPI +/- toe pressures as the screening tool.
- Hence the prevalence of peripheral arterial occlusive disease in this study was found to be 7.69%.
- Among the PAOD group, 17 (54.8%) were females and 14 (45.2%) were males.
- Among the PAOD group, 3 patients were found to have >25% reduction in post-exercise ABPI which was considered significant. But all these patients also had abnormal ABPI at rest or post exercise.

### **Results of bivariate analysis**

#### **Age and PAOD**

Variable	PAOD- YES	PAOD- NO	p value
Age	40.71 $\pm$ 8.46	41.51 $\pm$ 8.25	0.603

**Conclusion** – In bivariate analysis, age did not play a significant role in the prediction of PAOD.

#### **Sex and PAOD (peripheral arterial occlusive disease)**

Variable	PAOD - YES	PAOD - NO	p value
Male	14 (45%)	224 (60%)	0.128
Female	17 (55%)	148 (40%)	

**Conclusion** - In bivariate analysis, sex had no statistically significant association with development of peripheral arterial occlusive disease in HIV patients.

#### **Body mass index (BMI) and PAOD**

Variable	PAOD – YES	PAOD – NO	p value
BMI	21.59 $\pm$ 5.187	22.20 $\pm$ 3.99	0.429

**Conclusion** – BMI had no significance with respect to the prediction of PAOD in HIV patients.

### **Tobacco and PAOD**

Variable	PAOD - YES	PAOD - NO	p value
Tobacco – YES	4	75	0.364
Tobacco – NO	27	297	

**Conclusion** - In bivariate analysis, tobacco had no statistically significant association with peripheral arterial occlusive disease in HIV patients.

### **Alcohol and PAOD**

Variable	PAOD - YES	PAOD - NO	p value
Alcohol – YES	3 (10%)	55 (15%)	0.597
Alcohol - NO	28 (90%)	317 (85%)	

**Conclusion** - In bivariate analysis, alcohol had no statistically significant association with peripheral arterial occlusive disease in HIV patients.

### **Diabetes mellitus (DM) and PAOD**

Variable	PAOD - YES	PAOD - NO	p value
DM – YES	1 (10%)	31 (15%)	0.494
DM – NO	30 (90%)	341 (85%)	

**Conclusion-** In bivariate analysis, diabetes mellitus had no statistically significant association with peripheral arterial occlusive disease in HIV patients.

### **Hypertension (HTN) and PAOD**

Variable	PAOD - YES	PAOD - NO	p value
HTN – YES	5 (16%)	58 (16%)	1.000
HTN - NO	26 (84%)	313 (84%)	

**Conclusion** - In bivariate analysis, hypertension had no statistically significant association with peripheral arterial occlusive disease in HIV patients.

### **Blood pressure (BP) and PAOD**

Variable	PAOD- YES	PAOD- NO	p value
BP (mm Hg)	124.39 ± 17.71	126.40 ± 18.25	0.554

**Conclusion** – Total cholesterol, HDL cholesterol, LDL cholesterol, Triglycerides and Blood pressure were found to be no significant predictor of abnormal ABPI (PAOD).

### **History of dyslipidaemia and PAOD**

Variable	PAOD - YES	PAOD - NO	p value
Dyslipidaemia – YES	1 (3%)	17 (5%)	1.000
Dyslipidaemia - NO	30 (97%)	355 (95%)	

**Conclusion** - In bivariate analysis, history of dyslipidaemia had no statistically significant association with peripheral arterial occlusive disease in HIV patients.

#### **Total cholesterol and PAOD**

Variable	PAOD – YES	PAOD – NO	p value
Total Cholesterol	180.88 ± 38.63	164.82 ± 3.99	0.333

#### **HDL cholesterol and PAOD**

Variable	PAOD – YES	PAOD – NO	p value
HDL Cholesterol	39 ± 12.67	37.16 ± 12.34	0.686

#### **LDL cholesterol and PAOD**

Variable	PAOD – YES	PAOD – NO	p value
LDL Cholesterol	104.75 ± 27.71	96.27 ± 28.86	0.424

**Conclusion:** In bivariate analysis, total cholesterol, LDL cholesterol, HDL cholesterol had no statistically significant association with peripheral arterial occlusive disease in HIV patients.

**Ischemic heart disease (IHD)/acute coronary syndrome (ACS)/ angina/coronary artery disease (CAD) and PAOD**

Variable	PAOD - YES	PAOD - NO	p value
IHD/ACS/CAD – YES	0	3 (1%)	1.000
IHD/ACS/CAD - NO	31 (100%)	369 (99%)	

**Conclusion** - In bivariate analysis, presence of ischemic heart disease/acute coronary syndrome/ angina/coronary artery disease had no statistically significant association with peripheral arterial occlusive disease in HIV patients

**Cerebrovascular accidents (CVA)/Transient ischemic attacks (TIAs) and PAOD**

Variable	PAOD – YES	PAOD- NO	p value
CVA/TIA – YES	0	1 (1%)	1.000
CVA/TIA - NO	31 (100%)	371 (99%)	

**Conclusion** - In bivariate analysis, history of cerebrovascular accident (CVA) or transient ischemic attacks (TIAs) had no statistically significant association with peripheral arterial occlusive disease in HIV patients

#### Family history of vascular events/disease and PAOD

Variable	PAOD – YES	PAOD – NO	p value
F/H/O vascular events – YES	1 (3%)	8 (2%)	0.517
F/H/O vascular events - NO	30 (97%)	364 (98%)	

**Conclusion** – In bivariate analysis, family history of vascular events (like myocardial infarction, stroke) or vascular disease had no statistically significant association with peripheral arterial occlusive disease in HIV patients

#### Duration of HIV and PAOD

Variable	PAOD – YES	PAOD – NO	p value
Duration of HIV (months)	33.65 ± 61.50	35.08 ± 52.33	0.001

**Conclusion** – Duration of HIV was significantly associated with prediction of PAOD

#### Duration of HIV treatment (HAART) and PAOD

Variable	PAOD – YES	PAOD – NO	p value
Duration of HAART	29.11 ± 36.11	47.05 ± 37.23	0.001

**Conclusion** – Duration of treatment (HAART) was found to be a significant predictor of PAOD



#### Use of protease inhibitors (PIs) and PAOD

Variable	PAOD - YES	PAOD - NO	p value
PIs – YES	17 (57%)	105 (30%)	0.004
PIs – NO	13 (43%)	246 (70%)	

**Conclusion** – In bivariate analysis, use of protease inhibitors had statistically significant association (p value = 0.004) with peripheral arterial occlusive disease in HIV patients

#### Duration of treatment with protease inhibitors (PIs) PAOD

Variable	PAOD – YES	PAOD – NO	p value
Duration of PIs	9.57 ± 9.84	17.70 ± 17.50	0.018

Conclusion – Duration of treatment with protease inhibitors was found to be an important predictor of PAOD in HIV patient population

#### CD4 count and PAOD

Variable	PAOD – YES	PAOD – NO	p value
CD4 < 300	15 (48%)	109 (29%)	0.041
CD4 > 300	16 (52%)	263 (71%)	

**Conclusion** – In bivariate analysis, CD4<300 was had statistically significant association (p value = 0.041) with peripheral arterial occlusive disease in HIV patients

### Multivariate analysis

Based on the bivariate analysis of continuous as well as non-continuous variables, duration of HIV, treatment duration, use of protease inhibitors, CD4 count <300 were chosen for multivariate analysis.

Variables	Odds Ratio	95% C.I	P value
<b>Treatment Duration</b>	1.002	0.98, 1.03	0.889
<b>HIV Duration</b>	0.984	0.96, 1.08	0.189
<b>CD4 count</b> <b>&lt; 300</b> <b>&gt;300</b>	1.93 1	0.88, 4.23	0.101
<b>PI</b> <b>Yes</b> <b>No</b>	2.64 1	1.22, 5.74	0.014

In the multivariate analysis, following results were obtained:

1. Use of protease inhibitors (OR-2.64), low CD4 count <300 (OR-1.93) and prolonged duration of ART treatment (OR-1.002) were found to be associated with a higher risk of developing peripheral arterial occlusive disease in HIV positive population.
2. Among those, the only risk factor which attained statistical significance for causation of peripheral arterial occlusive disease was protease inhibitor use (p = 0.014).
3. In those with protease inhibitor use, duration of treatment with this agent was also found to be significantly associated (p = 0.018) with peripheral arterial occlusive disease

## **Chapter 6**

### **DISCUSSION**

Peripheral arterial occlusive disease is a well-known entity in all parts of the world. There are multiple risk factors which are described in literature to be associated with causation of this disease in general population. This includes smoking, diabetes mellitus, hypertension, prior history of cardiovascular events and family history of vascular disease/events.

It has been repeatedly proven that peripheral arterial occlusive disease is a marker of future cardiovascular events like stroke and myocardial infarction. Hence the recognition of this disease in the early stage is important with respect to the early initiation of therapy and also in helping to prevent the other cardiovascular morbidities.

Human immunodeficiency virus (HIV) causes AIDS. There are multiple presentations of this disease including opportunistic infections. HIV associated vasculopathy is well described in literature and most common aetiology for the same is atherosclerosis.

Prevalence of peripheral arterial occlusive disease in general population has been repeatedly studied. But there are only very few studies which had tried to identify the prevalence of this problem in HIV positive patients. This could probably be due to the under-recognition of this disease in this population. There is hardly any study from India where HIV is a growing problem of concern.

The morbidity and mortality associated with peripheral arterial occlusive disease in HIV population could be higher than that in the general population owing to the depressed immune system.

This study was designed as an attempt to address the above problem in an Indian setting. Peripheral arterial occlusive disease in HIV positive patients were studied using widely accepted definitions and standardised screening tools.

Symptomatology was assessed with the help of Edinburgh Claudication Questionnaire. Intermittent claudication was reported by 4.7% of study population. Among those with PAOD (n=31), 16.1% of patients reported PAOD. This was found to be statistically significant proving the strong association between “intermittent claudication” and presence of peripheral arterial occlusive disease in this population (p value - 0.011). This has been repeatedly proven in studies conducted in general population as well as in HIV population.

Another important point to be noted here is the fact that 83.9% patients with PAOD and HIV did not report intermittent claudication. These patients form the asymptomatic group. This point also has been repeatedly proved in studies that a major proportion of HIV positive patients with PAOD are asymptomatic. Hence it is very important to screen all HIV patients for PAOD, especially to pick up these asymptomatic ones. They can be managed largely with life style modifications, exercises or a change in drug regime.

Ankle brachial pressure index (ABPI) was used as the main screening tool to identify peripheral arterial occlusive disease. Patients who had high ABPI (suggesting non-compressible vessels) also required measurement of toe pressures to rule out PAOD.

Measurement of ABPI and toe pressures was according to standard protocols in the vascular laboratory attached to the Department of Vascular Surgery. Measurement of ABPI by a single investigator using same Doppler machine and blood pressure cuff helped eliminated inter-observer variability and probably helped reduce the intra-observer variability as well.

Study population involved patients from almost all age groups >18 years and the mean age was around 40. Among those with PAOD, the mean age was 40.71. This proves that the study involved significant number of patients on either side of this age which is a good representation of adult HIV positive patients.

Study involved about 41% female patients and 59% males. This showed a good representation of both sexes in the study. Hence the results of the study could be generalised as well.

Prevalence of peripheral arterial occlusive disease obtained in this study was about 7.69%. And this in comparison to other similar studies (mentioned above) again proved that the prevalence of this disease in this population could be more than what is thought. And more over this could probably be the only large scale study from India which addressed the problem in this particular population. Prevalence of PAOD in general population was found to be about 1% at 50 years and about 3% at 60 years. Considering this data, the high prevalence obtained in this study could be alarming. This means that these patients are at high risk of other cardiovascular morbidities in the future as well in comparison to general population. Hence a comprehensive system needs to be formulated to address this issue in this population.

Post exercise modification of ABPI had helped many researchers in identifying milder/dormant forms of occlusion. My study also assessed ABPI with a post exercise modification as mentioned earlier. This definitely had helped in identifying more cases of PAOD. Utilisation of this modality has been repeatedly proven to be of help in identifying more asymptomatic patients. Many studies which utilised this modification have found a higher prevalence of peripheral arterial occlusive disease in HIV patients, in comparison to studies which have not utilised the same.

Traditional risk factors associated with peripheral arterial occlusive disease includes:

Diabetes mellitus, smoking, hypertension, obesity, metabolic syndrome, prior cardiovascular disease, family history of vascular disease/cardiovascular events.

It has been shown in many studies that these traditional risk factors are not prevalent in HIV positive PAOD patients. This study also found a similar result. None of the traditional risk factors were found to be significant in the univariate or multivariate analysis for the causation of PAOD in this population. This could mean that the patient selection for screening should not include only those with traditional risk factors. In fact it is prudent to include all HIV positive patients irrespective of the presence or absence of traditional risk factors.

So it could be proposed that all HIV patients need to be screened for presence of peripheral arterial occlusive disease since the prevalence is high and also the prevention as well as treatment could be initiated at the earliest.

Another important link to the development of PAOD in HIV patients is the use of HAART. After the introduction of HAART (Highly Active Anti-Retroviral Therapy), the morbidity and mortality of HIV and associated opportunistic infections has significantly reduced. Many studies have repeatedly proved the development of various metabolic abnormalities secondary to HAART therapy. This included metabolic syndrome, insulin resistance, and dyslipidaemia. And as we all know, all these factors have been well described in literature to be the aetiological agents for any cardiovascular disease including peripheral arterial occlusive disease.

This study also was aimed at finding any similar association. Among all class of ART agents, use of protease inhibitors was found to be associated with PAOD. These drugs in comparison to other ART drugs cause significant metabolic derangements. Our final analysis has showed that there is statistically significant association (p value- 0.011) between use of protease inhibitors and development of PAOD.

Most of our patients who were receiving protease inhibitors were using “tenofovir”. Whether other protease inhibitors also have a similar association need to be proved in large scale epidemiological studies.

Certain studies also had proved that the duration of treatment with protease inhibitors also is equally important in the causation of PAOD. Average duration of treatment with protease inhibitors in our study was 16.57 months.



Many of these patients who were on this drug had never had their lipid profile being checked. This study helped us initiate lipid profile screening for all these patients.

The higher prevalence of PAOD in this population could be due to many reasons. First of all it could be related to a direct virus induced endothelial dysfunction resulting in vascular disease. This is the reason most commonly being postulated for HIV induced vasculopathy. Various mechanisms by which this endothelial dysfunction develops is being described in detail elsewhere. With respect to this, it is important to note that duration of HIV had showed some significant association to the development of PAOD in bivariate analysis. This could probably mean that repeated and persistent endothelial dysfunction could result from prolonged duration of HIV infection. But this association has to be proved stronger in large scale studies with more number of patients.

Another important distinction to be made is whether there is a difference of prevalence in patients who are receiving HAART in comparison those who have never received the same. This could probably help us prove a direct role of virus itself in the causation of PAOD. But this becomes difficult as most patients with HIV are being on treatment for the same and doing a comparative study in that setting may be challenging.

CD4 count has been found to be a risk factor for development of PAOD. Many studies including Periard et al (74) have shown that HIV patients with low CD4 counts have an increased risk of developing PAOD. The cut off used has varied. In our study also, a higher risk of developing PAOD was found in those patients with CD4 count <300 in comparison to those with CD4 counts >300. But in multivariate analysis, it lost significance ( $p = 0.101$ ).

Even then the risk (OR-1.93) was high. This could mean that the endothelial dysfunction or the degree of inflammation which happens in the vessel could be more in those with a suppressed immune system. Large scale studies are further required to strongly prove this association.

Overall the study helped prove the higher prevalence of PAOD in HIV positive patients as described in limited western studies. It also provided an insight into the possible specific risk factors which could be associated with development of PAOD in this population. This will definitely help in formulating large scale epidemiological studies in this part of the world.

## **Chapter 7**

## **CONCLUSIONS**

## **Conclusions**

1. Prevalence of peripheral arterial occlusive disease in HIV positive patients is about 8 %.

This in comparison to data among general population is high.

2. The risk factors for PAOD in HIV positive patients which attained statistical significance at the end of the study were;

- Use of protease inhibitors
- Duration of treatment with protease inhibitors

3. In the univariate analysis, following risk factors were also found to be significant, but they did not correlate well in the multivariate analysis:

- Duration of HIV infection
- Treatment (HAART) duration
- CD4 count < 300

4. Traditional risk factors for peripheral arterial occlusive disease (like DM, HTN, dyslipidaemia, smoking) were not contributing significantly to the causation of peripheral arterial occlusive disease in HIV positive population.

5. Risk factors associated with higher risk of PAOD in this population was not much different from that of western population. But smoking, DM and age which attained statistical significance in many studies in the west were not significant in this study, even in the bivariate analysis.

## **Chapter 8**

### **LIMITATIONS**

## Limitations

1. Study was conducted by a postgraduate student. Time constraints were the major limitation which prevented me from recruiting consecutive patients into the study. Hence the estimated prevalence might not reflect the true prevalence in the community. Hence large scale community based epidemiological studies with more number of patients are required to estimate the true prevalence of this disease in HIV patients.
2. Stigma of the patient – The stigma associated with HIV disease is more than what I thought. This has played a major role in my study especially with respect to the blood investigations (especially lipid profile) and further evaluations. Even though a large number of patients were on protease inhibitors, they never had a lipid profile tested. Those patients especially who were positive for PAOD were offered lipid profile testing free of cost by providing fund from my study. They were also referred to the Vascular Surgery Unit of our hospital for further evaluations and treatment. But the common reply I received was that “they cannot wait for that” or “cannot come for that tomorrow” or “someone might see them hanging around in hospital”. This has resulted in me not getting enough data to identify those who were having undiagnosed dyslipidemia which is a major risk factor for PAOD in any patients and especially in an HIV patient on protease inhibitors.

3. Confirmation of the disease – Even though ABPI and Toe pressures have good sensitivity and specificity in identifying clinically relevant occlusions of the vessels, they are not the gold standard for identification of PAOD. It is the Doppler and angio studies which are considered the gold standards for detection of PAOD. And more over they help us in identifying the level and nature of occlusion and help us plan the treatment. But my study did not had a provision for Doppler or angiographic studies for the patients due to large finances included. But those patients who were found to have PAOD from my study were referred to Vascular Surgery unit for further evaluations which included one of these gold standard tests. But as I mentioned earlier, majority had not turned up for the same due to stigma from the disease and also due to the large cost involved in further evaluations and treatment.
  
4. Temporal ambiguity – Peripheral arterial occlusive disease might have been presented in a particular HIV positive patient before he/she was diagnosed with HIV. So in those patients, whether HIV has contributed to the causation of PAOD may be difficult to predict. This will remain a limitation of my study.



## **Chapter 9**

### **POTENTIAL FOR FURTHER RESEARCH**

## **POTENTIAL FOR FURTHER RESEARCH**

1. This study probably is the first study of its kind from India addressing the problem of PAOD in HIV patients. This can help other researchers formulate similar studies which will definitely benefit our HIV population
2. Time constraints of a postgraduate student limited the number of patients in the study. Same study can be continued further by including more number of patients. This could strengthen the power of study as well. The setting provides enough and more patients to develop this into a large scale study.
3. Study can also be extended into the community so as to help identify the true prevalence. ART registry in the ART clinic could help us identify all patients under the locality. But it may be a cumbersome process to trace these patients to their locality especially with the amount of stigma they live with.
4. More risk factors could be studied (like viral load, type of protease inhibitor)
5. Studies could be framed so as to correlate an abnormal ABPI with Doppler findings. This will prove those patients who truly have PAOD. Even though the sensitivity of ABPI in diagnosing PAOD is high, it is only a screening tool and not a gold standard. This study was limited by the fact that there was no provision for further evaluation of PAOD patients to prove true PAOD with the help of Doppler. This was due to the constraints of the study

being a thesis. Hence further research with more financial support could pave way for including Doppler confirmation of PAOD in those with an abnormal ABPI.

6. Study was limited by the fact that, none of the patients who were diagnosed with PAOD could be given any treatment/interventions. This needed confirmation, localisation of disease if it was confirmed and further investigations (CT/MR angio/ECHO). There was no provision for these in this study for any of these. Even though these were offered to all PAOD patients, most did not turn up to the vascular clinic, probably due to the large finances involved in all these. And in an Indian setting, finance plays a major role in availing treatment. And this is of importance in this particular group since majority are unemployed (due to the social stigma which still prevail this part of the world). Hence studies which could incorporate higher evaluations and interventions if required need to be formulated for benefitting PAOD patients in this population.

## **ANNEXURE 1**

### **PATIENT INFORMATION SHEET**

**Christian Medical College and Hospital, Vellore**

**Department of General Surgery**

**PATIENT INFORMATION SHEET - THE PAODH STUDY (Prevalence and risk factors of Arterial Occlusive Disease in HIV positive patients)**

- 1) WHAT IS HIV? HIV is a virus causing immune system breakdown in our body. There is no cure for this condition. But it can be treated well these days which can extend your life.
- 2) WHAT IS PERIPHERAL VASCULAR SYSTEM? The blood vessels which supplies and takes away blood from our legs and arms comprises peripheral vascular system
- 3) WHAT IS PERIPHERAL ARTERIAL OCCLUSIVE DISEASE? A block in one or many of your peripheral artery(s) can stop the blood supply and hence nutrition to the leg/arm. This can develop slowly or suddenly in a short time.
- 4) WHAT ARE ITS CONSEQUENCES? If there is a block to blood supply, then cells will die either slowly or suddenly. It can lead to skin changes, ulcers, pain in the leg while walking, loss of sensation, paresis and ultimately limb loss.
- 5) HOW IS HIV RELATED TO THIS? HIV can affect your blood vessels badly in the way described above and can lead to the above consequences. So if you are screened early for the presence of "BLOCK" in your blood vessels, there are ways to rectify or modify the "BLOCK"
- 6) WHAT IS THIS STUDY ABOUT? This study will check the blood pressure in your arms and legs after resting and after a short stint of walking. It will then let you know whether you have a block in your blood vessels or not.
- 7) WHAT ARE THE RISKS AND BENEFITS TO ME IF I TAKE PART? There are no risks involved in this study. Only benefits as this will detect a block in your blood vessels in short time with just few blood pressure measurements.
- 8) WHAT NEXT IF THERE IS A BLOCK TO MY VESSEL? We will lead you to do further tests/ advice you to undergo corrective measures to remove block in blood vessel either with the help of medicines and or surgery.
- 9) CAN I WITHDRAW FROM THE STUDY AFTER SIGNING CONSENT FORM? You can always withdraw from the study at any point of time
- 10) WILL MY NAME AND PERSONAL DETAILS BE PUBLISHED/GIVEN TO A THIRD PARTY? Your name and personal details will be kept confidential.
- 11) WHOM CAN I CONTACT IF I HAVE ANY MORE QUERIES? Dr. Suraj.S, Department.of General Surgery -IV during working hours or at [suraj.cmc@gmail.com](mailto:suraj.cmc@gmail.com)/04162282441

## **ANNEXURE 2**

### **INFORMED CONSENT FORM**

**Christian Medical College and Hospital, Vellore**

**Department of General Surgery**

**THE PAODH STUDY (Prevalence and risk factors of Arterial Occlusive Disease in  
adult HIV positive patients)**

Patient name:                      Sex:                      Age:                      Hospital number:  
Study code no:  
Date:

With regard to the procedure:

I confirm that I have explained the indications, benefits and common risks. I have done this in terms and language which in my judgment is suited to the understanding of the patient.

Name of the doctor:

Signature with Employment no/registration number:

Patient

I voluntarily agree to take part in this study.

The doctor named in this form has explained the benefits and risks of the proposed study to me.

I voluntarily agree to be part of the above said study in person.

I declare that I have read the information sheet provided to me regarding this study and have clarified any doubts that I had. I do understand what HIV is and what are its after effects especially related to blood vessels. I understand the need for such a study and how it will be useful to myself and others having similar disease.

I also understand that my participation in this study is entirely voluntary. I understand that I have full right to reject my participation or withdraw permission to continue at any time without affecting my usual treatment or my legal rights.

I understand that I will not receive any other financial compensation.

I understand that my identity will not be relieved in any information released to third parties or published.

I agree to clinical photographs being taken during the course of my stay in hospital. I know that my identity will be protected and that this will be used only for educational purposes.

I know that there lies a possibility of evaluations and or interventions based on the above said study which has its own benefits and risks which are clearly being explained to me by the doctor. I do understand that those evaluations and interventions will only be done if I voluntarily choose to undergo the same as it is not included as part of the current study I'm signing into. I also understand that the expenses of further tests or interventions will have to be borne by me.

Patient:	Name:	Signature:	Date:
Investigator:	Name:	Signature:	Date:
Witness:	Name:	Signature:	Date:

## **ANNEXURE 3**

### **PROFORMA**



**Christian Medical College, Vellore**

**Department of General Surgery**

**PROFORMA - THE PAODH STUDY (Prevalence and risk factors of Arterial Occlusive Disease in HIV positive patients)**

Name:                      Age:                      Sex: M/F (Circle appropriate)

Hospital no:                      Study Code no: 10001

**.SYMPTOMATOLOGY**

Claudication: Yes/No (Based on Edinburgh questionnaire)      Duration: ----- years/months/days

Claudication distance : ----- feet/meters/kilometers

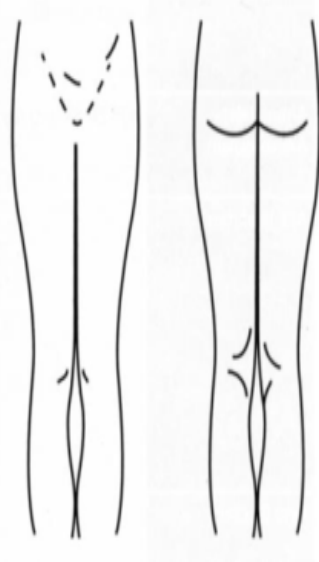
Site of claudication:

Rest pain: Yes/No      Duration: ----- years/months/days

Ulcers/gangrene/amputation: Yes/No (circle appropriately)      Duration: ---- years/days/months

**The Edinburgh Claudication Questionnaire:**  
**CAD/PVD**

\* A positive questionnaire diagnosis of claudication is made only if the “**correct**” answer is given to **all questions**

Questions	Correct Answer	
1. Do you get pain or discomfort in your legs(s) when you walk? <input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unable to walk • If you answered “yes” to question 1, please answer the following questions	Yes	
2. Does the pain ever begin when you are standing or sitting still?	No	
3. Do you get it when you walk uphill or in a hurry?	Yes	
4. Do you get it when you walk at an ordinary pace on the level?	Yes	
5. What happens if you stand still? • Usually continues for more than 10 minutes? • Usually disappears in 10 minutes or less?	No Yes	
6. Where do you get this pain or discomfort? • Mark the places with an “X” on the diagram		

## RISK FACTORS

Tobacco: Present/Absent

PRODUCT	YEARS OF USE

Alcohol: Present/Absent

Years of use:

Diabetes: Present/Absent

Years:

Hypertension: Present/Absent

Years:

Dyslipidemia: Present/ Absent

Years:

CVA/MI/ANGINA/ANEURYSMS: Present/Absent

Years:

(Circle appropriately)

Family history of any of above : Present/ Absent

Years:

## PRIMARY DISEASE&TREATMENT DETAILS

Duration since HIV diagnosed: ----- years/months

Duration on ART: ----- years/months

Regular on treatment: Yes/ No

History of treatment with protease inhibitors (Either currently on it/was on it in past):Yes/No

Duration of treatment with protease inhibitors: ----- years/months

## Details of treatment

SL NO	DRUG NAME	DURATION(yrs/months)

### CLINICAL PARAMETERS

Height -                                      Weight –  
BMI -  
Pulse rate -                                      Blood pressure –

#### Clinical pulses

SITE	RIGHT	LEFT
Radial		
Ulnar		
Brachial		
Femoral		
Popliteal		
Posterior tibial		
Dorsalis pedis		
Carotid		
Carotid bruit		

+++ bounding ++ Strong, + weak, - absent, c/m – Can't be measured (amputated)

### LABORATORY INVESTIGATIONS

Haemoglobin:

Lipid profile:

Total cholesterol:

Triglyceride level:

HDL cholesterol:

LDL cholesterol:

CD4 count :

Serum albumin:

### PARAMETER MEASUREMENT

PARAMETER	RIGHT	LEFT
REST ABPI		
POST EXERCISE ABPI		
TOE PRESSURE (if needed)		
TBI (if needed)		

Name of investigator/doctor:

Date and time:

Signature:

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NAME	AGE	SEX	CLAUD	DISTANCE	REST PAIN	CLI	TOBACCO
Kannamma	45	1	1	2	0	0	0
Saraswathi	49	1	0 -	-	-	-	0
Kamala	55	1	0 -	-	-	-	0
Issac.D	40	0	0 -	-	-	-	0
Ramya	18	1	0 -	-	-	-	0
Dharman	58	0	1	3	0	0	1
Venkatesan	47	0	1	0.5	0	0	1
Saravanan	35	0	0 -	-	-	-	0
Aruna	46	1	0 -	-	-	-	0
Neelamaken	42	0	0 -	-	-	-	0
Ravichandran	49	0	0 -	-	-	-	0
Vino.S	26	1	1	1	0	0	0
Kamesh	47	0	1	1	0	0	0
Prabhavathy	30	1	0 -	-	-	-	1
Mohanbabu	52	0	1	0.1	0	0	1
H.Naidu	60	0	0 -	-	-	-	1
Omprakash	32	0	0 -	-	-	-	1
Andal	46	1	0 -	-	-	-	0
Janakiraman	40	0	0 -	-	-	-	0
Alice	45	1	0 -	-	-	-	0
Glory	44	1	0 -	-	-	-	0
Raja	45	0	0 -	-	-	-	0
Geetha	35	1	0 -	-	-	-	0
Baby	46	1	0 -	-	-	-	1
Anbu	47	0	0 -	-	-	-	0
Narayanamoorthy	42	0	0 -	-	-	-	0
Govindaraj	55	0	0 -	-	-	-	1
Balaji	40	0	0 -	-	-	-	1
Jyothi	35	0	0 -	-	-	-	1
Chennakrishna	44	0	0 -	-	-	-	0
Gopalan	50	0	1	0.5	0	0	0
Suresh	38	0	0 -	-	-	-	0
Sekar	47	0	0 -	-	-	-	1
Dharani	50	1	0 -	-	-	-	0
Shanthi	42	0	1	1	0	0	0
Jayakantha	39	0	0 -	-	-	-	0
Meenakshi	40	1	0 -	-	-	-	0
Latha	36	1	0 -	-	-	-	0
Dhandapani	37	0	0 -	-	-	-	0
Manogaran	48	0	0 -	-	-	-	0
Chitra	32	1	0 -	-	-	-	1
Chithra	35	1	0 -	-	-	-	0
Harikrishna	60	0	0 -	-	-	-	1
Arun Kr	29	0	0 -	-	-	-	0
Ravichandran	46	0	0 -	-	-	-	1
Jagan	37	0	0 -	-	-	-	1
Ravi	47	0	0 -	-	-	-	0
Vasantha Kr	32	0	0 -	-	-	-	0
Sankaraih	33	0	0 -	-	-	-	0

Basant.Kr	43	0	0 -	-	-		0
Palaniswamy	41	0	0 -	-	-		0
Narasimman	41	0	0 -	-	-		1
Siva	39	0	0 -	-	-		1
Arul.A	40	0	0 -	-	-		1
Selvam	43	0	1	1	0	0	0
Chithra	34	1	0 -	-	-		0
Savithri	39	1	0 -	-	-		0
Victor	49	0	1	1	0	0	0
Savithri	45	1	0 -	-	-		0
Ramesh	43	0	0 -	-	-		0
Kumuravalli	52	1	0 -	-	-		0
Padma	35	1	0 -	-	-		0
Velu	36	0	0 -	-	-		1
Santhi	42	1	0 -	-	-		0
Indhumathi	29	1	0 -	-	-		0
Chandran	36	0	0 -	-	-		0
Samsath.B	40	1	0 -	-	-		0
Thamara	32	1	0 -	-	-		0
Arunachalam	40	0	0 -	-	-		1
Shanthi	50	1	0 -	-	-		0
Geetha	37	1	0 -	-	-		0
Devaki	56	1	0 -	-	-		0
Sanjay	46	0	1	2	-		1
Arunachalam	60	0	0 -	-	-		0
Arumugam	39	0	0 -	-	-		0
Ravi	38	0	0 -	-	-		0
Ravi	47	0	0 -	-	-		0
Venkatesan	43	0	0 -	-	-		1
J.Venkatalakshmi	42	1	0 -	-	-		0
Velmurugan	37	0	0 -	-	-		1
Madhaiyan	49	0	0 -	-	-		0
Venkataramanah	62	0	0 -	-	-		1
Samuel	36	0	0 -	-	-		1
Loganathan	46	0	0 -	-	-		1
K.Jyothi	42	1	0 -	-	-		0
Murugan	39	0	0 -	-	-		0
Revathi	29	1	0 -	-	-		0
Jagadeswari	38	1	0 -	-	-		0
Jothi	34	1	0 -	-	-		0
Easwari	42	1	0 -	-	-		0
Kavitha	35	1	0 -	-	-		1
Murugan	44	0	0 -	-	-		0
Shiv Kumari	44	1	0 -	-	-		0
Kavitha	44	1	0 -	-	-		0
Audiyappan	55	0	0 -	-	-		0
Bijay Shankar	45	0	0 -	-	-		1
Deenadayalan	40	0	0 -	-	-		1
Chinnabba	46	1	0 -	-	-		0
Tamilmani	53	0	0 -	-	-		0

A.Venkataram	30	0	0 -	-	-	0
Logesh	49	0	0 -	-	-	1
Ramu	34	0	0 -	-	-	0
Manju Gupta	35	1	0 -	-	-	0
Murali	39	0	0 -	-	-	0
Tanzila Bibi	40	1	0 -	-	-	0
H.S.Mondal	47	0	0 -	-	-	1
Meenatchi	48	1	0 -	-	-	0
Murthy	27	0	0 -	-	-	1
Thangadurai	40	0	0 -	-	-	1
Govindaraj	46	0	0 -	-	-	1
Malarvizhi	37	1	0 -	-	-	0
Anjaneyalu Reddy	55	0	0 -	-	-	0
Sasikala	21	1	0 -	-	-	0
Meenatchi	45	1	0 -	-	-	0
Meenachi	42	1	1	0.5 -	-	0
Anitha	25	1	0 -	-	-	0
Perumal	43	0	0 -	-	-	0
Selvi	39	1	0 -	-	-	0
Jyothi	35	1	0 -	-	-	0
Kasthuri	26	1	0 -	-	-	0
Chithra	37	1	0 -	-	-	0
Suresh	44	0	0 -	-	-	0
Murugesan	46	0	0 -	-	-	0
Yesupadam	48	0	0 -	-	-	0
Vijaya	50	1	0 -	-	-	0
Arumugam	56	0	0 -	-	-	0
Usha	46	1	0 -	-	-	0
Asha devi	53	1	0 -	-	-	0
SelvaKr	43	0	0 -	-	-	0
Anandan	43	0	0 -	-	-	0
Ramesh	38	0	0 -	-	-	0
Rajesh Kr	43	0	0 -	-	-	1
Sriram Kr	35	0	0 -	-	-	0
Karunakaran	43	0	0 -	-	-	0
Balaji	29	0	0 -	-	-	0
Sakthivel	30	0	0 -	-	-	0
Kondreddy	58	0	0 -	-	-	0
Ramachandran	50	0	0 -	-	-	0
Vimala	43	1	0 -	-	-	0
Uma Mageswari	28	1	0 -	-	-	0
Balaji.D	40	0	0 -	-	-	0
Thangaraj	40	0	0 -	-	-	1
Omprakash	33	0	0 -	-	-	1
Venkateswarulu	35	0	0 -	-	-	0
Bujamma	34	1	0 -	-	-	0
Kumar	41	0	0 -	-	-	1
Elumalai	42	0	0 -	-	-	0
Sivakumar	43	0	0 -	-	-	0
Subramani	40	0	0 -	-	-	0

Vijayan	46	0	0 -	-	-		0
SekharD.R	40	0	0 -	-	-		0
Vadivel	43	0	0 -	-	-		0
Mahadevan	42	0	0 -	-	-		1
Anandhi	35	1	0 -	-	-		0
Ammu	25	1	0 -	-	-		0
George	33	0	0 -	-	-		0
Krishnankutty	39	0	0 -	-	-		0
Saravanan	38	0	0 -	-	-		0
Ratinakumari	39	1	0 -	-	-		0
Suguna	29	1	0 -	-	-		0
Satish	35	0	0 -	-	-		0
Janakiraman	40	0	0 -	-	-		0
Jagadheesh	46	0	0 -	-	-		0
Sudheer Kumar	42	0	0 -	-	-		0
Giridhar	48	0	1	1	0	0	0
Meena	36	1	0 -	-	-		0
Sreenivasa Reddy	46	0	0 -	-	-		1
Chitti Babu	47	0	0 -	-	-		1
Sridhar	49	0	0 -	-	-		0
Parimala	31	1	0 -	-	-		0
Clarence	42	0	0 -	-	-		0
Balamurugan	34	0	0 -	-	-		0
Indra	42	1	0 -	-	-		0
Suresh	33	0	0 -	-	-		0
Srinivasan	52	0	0 -	-	-		1
Kumar	49	0	0 -	-	-		0
Varadharajan	50	0	0 -	-	-		1
Suresh	34	0	0 -	-	-		0
Devika	46	1	0 -	-	-		0
Krishnan	54	0	0 -	-	-		0
Senthamarai	60	1	0 -	-	-		0
Mahalakshmi	28	1	0 -	-	-		0
Aanumakka	60	1	0 -	-	-		0
Sampath	43	0	0 -	-	-		0
Soundararajan	48	0	0 -	-	-		0
Elumalai	52	0	0 -	-	-		0
Abdula Kalam	52	0	0 -	-	-		0
Murugan	35	0	0 -	-	-		1
Ravi	45	0	0 -	-	-		0
Ranganathan	45	0	0 -	-	-		0
Christopher	54	0	0 -	-	-		0
Vekatesh	44	0	0 -	-	-		0
Shanthi	27	1	0 -	-	-		0
Ramakrishna Yadav	48	0	1	1	0	0	0
Arun Raj	27	0	0 -	-	-		0
Rajalakshmi	42	1	0 -	-	-		0
Sujatha	34	1	0 -	-	-		0
Srinivasa Naidu	40	0	0 -	-	-		0
Usha	34	1	0 -	-	-		0



Vijaya	32	1	0 -	-	-		0
Damodharan	40	0	0 -	-	-		0
Jouher	45	0	0 -	-	-		0
Selvi	45	1	0 -	-	-		0
Raja.M	29	0	0 -	-	-		0
Tamizharasu	40	0	0 -	-	-		0
Muthukrishnan	49	0	0 -	-	-		0
Sivakumar	42	0	0 -	-	-		0
Valarmathi	44	1	0 -	-	-		0
Kumaran	37	0	0 -	-	-		0
Lalitha	37	1	0 -	-	-		0
Arumugam	48	0	0 -	-	-		0
G.Ravi	44	0	0 -	-	-		1
Ganesh	48	0	0 -	-	-		0
Kumari	37	1	0 -	-	-		0
Govindaraj	33	0	0 -	-	-		1
Kesavan	46	0	1	0.5	0	0	0
Mannuswamy	69	0	0 -	-	-		0
Lavanya	30	1	0 -	-	-		0
Mahesh	40	0	0 -	-	-		0
Ramachandran	38	0	0 -	-	-		0
Kannan	43	0	0 -	-	-		1
Srinivasan	43	0	0 -	-	-		0
Manjula	34	1	0 -	-	-		0
Sumathi	40	1	0 -	-	-		0
Esther	37	1	0 -	-	-		0
Rajathi	34	1	0 -	-	-		0
Shobha	37	1	0 -	-	-		0
Sugumar.S	32	0	0 -	-	-		0
Siva	43	0	0 -	-	-		1
Shakila	46	1	0 -	-	-		0
Booma Devi	46	1	0 -	-	-		0
Jeyaraman	51	0	0 -	-	-		0
Murugaiyan	39	0	0 -	-	-		0
Chandrika	40	1	0 -	-	-		0
Subba reddy	59	0	0 -	-	-		0
Vanitha	38	1	1	1	0	0	0
Gunavathi	40	1	0 -	-	-		0
Srinivasan	50	0	0 -	-	-		1
Jothi	26	1	0 -	-	-		0
Veerammal	46	1	0 -	-	-		0
Andiappan	58	0	0 -	-	-		0
Anuj Singh	46	0	0 -	-	-		0
Solai	43	0	0 -	-	-		1
Kumar	32	0	0 -	-	-		0
Chithra.M	33	1	0 -	-	-		1
Arockiadas	70	0	0 -	-	-		1
Vairakannu	45	0	0 -	-	-		0
Balasubaiah	41	0	0 -	-	-		1
Kumari	38	1	0 -	-	-		0

Loganathan	41	0	0 -	-	-		0
Kumar	40	0	0 -	-	-		0
Arumugam	57	0	0 -	-	-		1
Suguna	35	1	0 -	-	-		0
Ananda Kumar	46	0	0 -	-	-		0
Kalpana	27	1	0 -	-	-		0
Kumar	36	0	0 -	-	-		0
Bharathi	47	1	0 -	-	-		0
Kotteswari	45	1	0 -	-	-		0
Saravanan	39	0	0 -	-	-		0
Thanjiyappan	38	0	0 -	-	-		0
Mohana	40	1	0 -	-	-		0
Munikannan	48	0	0 -	-	-		0
Murali	39	0	0 -	-	-		0
Jayashankar	47	0	0 -	-	-		1
Sigamani	29	0	0 -	-	-		0
Raja	42	0	0 -	-	-		0
Muniswamy	48	0	0 -	-	-		0
Saraswathi	48	1	0 -	-	-		0
Sivasangari	31	1	0 -	-	-		0
Venkatesan	40	0	0 -	-	-		1
Ganeshan	40	0	0 -	-	-		0
Subramanyam	38	0	1	0.5	0	0	0
Rathinavel	38	0	0 -	-	-		0
Lavanya	22	1	0 -	-	-		0
Krishnan	55	0	0 -	-	-		1
Prabha Rani	32	1	0 -	-	-		0
Govindaraj	42	0	0 -	-	-		0
Vijay	40	0	0 -	-	-		0
Jaya	33	1	0 -	-	-		0
Geetha	38	1	0 -	-	-		0
Mohan	42	0	0 -	-	-		0
Lucky	40	0	0 -	-	-		1
J.V.Lakshmi	42	1	0 -	-	-		0
Kousalya	33	1	0 -	-	-		0
Babu	48	0	0 -	-	-		1
Moorthy	47	0	0 -	-	-		0
Jeyakumar	39	0	0 -	-	-		1
Prabhakar Naidu	40	0	0 -	-	-		0
Kavitha	28	1	0 -	-	-		0
Gajalakshmi	43	1	0 -	-	-		0
Selvi	38	1	0 -	-	-		0
Bharathi	42	1	0 -	-	-		0
Sathyalakshmi	40	1	0 -	-	-		0
Girija	37	1	0 -	-	-		0
Kalaiselvi	48	1	0 -	-	-		0
Manimegalai	28	1	0 -	-	-		0
Jennima.F	29	1	0 -	-	-		0
Neelavalli Shobhana	27	1	0 -	-	-		0
Malarkodi	47	1	0 -	-	-		0

Kasthuri	35	1	0 -	-	-	0
N.Mahesh	33	0	0 -	-	-	0
Ganeshan	59	0	0 -	-	-	1
Somasundaram	49	0	0 -	-	-	0
Chitra	35	1	0 -	-	-	0
Boopathi	40	0	0 -	-	-	0
Rajeswari	40	1	0 -	-	-	0
Shankar	49	0	0 -	-	-	0
Rajesh Kr	32	0	1	1 -	-	1
Sujata	36	1	0 -	-	-	0
Geetha	36	1	0 -	-	-	0
Shanthi	40	1	0 -	-	-	0
Renuka	48	1	0 -	-	-	0
Bharathi	40	1	0 -	-	-	0
Arun.S	27	0	0 -	-	-	0
Sumathi	47	1	0 -	-	-	0
Ponnuswamy	51	0	0 -	-	-	1
Shanthi	53	1	0 -	-	-	0
Premlatha	36	1	0 -	-	-	0
Ezhumalai	45	0	0 -	-	-	0
Banumathi	55	0	0 -	-	-	0
Dhamodharan	45	0	0 -	-	-	0
Raman	49	0	0 -	-	-	0
Thulukkanan	45	0	0 -	-	-	0
Sathish Kr	38	0	0 -	-	-	0
Nagarajan	43	0	0 -	-	-	0
Thirumugam	51	0	0 -	-	-	0
Renuka	36	1	0 -	-	-	0
Kalaivani	50	1	0 -	-	-	0
Mohan	44	0	0 -	-	-	0
Parimala	43	1	0 -	-	-	0
Banumathi	37	1	0 -	-	-	0
Pownammal	50	1	0 -	-	-	0
Amsa	50	1	0 -	-	-	0
Babu	43	0	0 -	-	-	0
Srinivasan	41	0	0 -	-	-	0
Vanitha	36	1	0 -	-	-	0
Pandiyan	49	0	0 -	-	-	0
Murugan	41	0	0 -	-	-	1
Valarmathi	45	1	0 -	-	-	0
Manogaran	53	0	0 -	-	-	0
Srinivasan	47	0	0 -	-	-	1
Rajalakshmi	24	1	0 -	-	-	0
Palani	32	0	0 -	-	-	0
Bhuvaneswari	36	1	0 -	-	-	0
Manjula	40	1	0 -	-	-	0
Amsa	40	1	0 -	-	-	0
Velmurugan	40	0	0 -	-	-	0
Mallesh	39	0	0 -	-	-	0
Sumathi	42	1	0 -	-	-	0

Reshma	37	1	0 -	-	-	0
Malarkodi	35	1	0 -	-	-	0
Clement	45	0	0 -	-	-	0
Chitti Babu	42	0	0 -	-	-	0
Gandhi	34	0	0 -	-	-	1
Annapoorni	55	1	0 -	-	-	0
Suseela	39	1	0 -	-	-	0
Syamala	42	1	0 -	-	-	0
Ealumalai	43	0	0 -	-	-	0
Revi	41	0	0 -	-	-	0
Lakshmi	33	1	0 -	-	-	0
Geetha	41	1	0 -	-	-	0
Thirumal	25	0	0 -	-	-	0
Ganapathy	48	0	0 -	-	-	1
Venugopal	58	0	0 -	-	-	1
Prabhavathy	32	1	0 -	-	-	0
Ramu	36	0	0 -	-	-	0
Kasthuri	53	1	0 -	-	-	0
Lokeswari	31	1	0 -	-	-	0
Balu	64	0	0 -	-	-	1
Srinivasan	45	0	0 -	-	-	1
Chitra	35	1	0 -	-	-	0
Meenkodi	23	1	0 -	-	-	0
Ramani	50	1	0 -	-	-	0
Elangovan	37	0	0 -	-	-	0
Meenakshi	40	1	0 -	-	-	0
Jyothi	43	0	0 -	-	-	1
Ramesh Babu	43	0	0 -	-	-	1
Varadhan	60	0	1	1	1	0
Jeyanthi	32	1	0 -	-	-	0
Srinivasan	61	0	0 -	-	-	1
Sivakumar	40	0	0 -	-	-	0
Girija	48	1	0 -	-	-	0
Venkatesh	43	0	0 -	-	-	1
Amulu	43	1	0 -	-	-	0
Sheela	42	1	0 -	-	-	0
Tamarai Selvi	44	1	0 -	-	-	0
Shimla Devi	45	1	0 -	-	-	1
Shaik Md Ali	46	0	0 -	-	-	1
Siva	46	0	0 -	-	-	0
Venkatesan	49	0	0 -	-	-	0
Selvam	55	0	0 -	-	-	1
Prema	31	1	0 -	-	-	0
Mical	47	0	0 -	-	-	0
Sanjay Bajaj	31	0	0 -	-	-	0
Sivaprakasam	55	0	0 -	-	-	0
Dhanalakshmi	28	1	0 -	-	-	0
Kalaivani	23	1	0 -	-	-	0
Murthy	35	0	0 -	-	-	0
T.S.Rao	37	0 -	-	-	-	0

Prameela	41	1	0 -	-	-	0
Emi.M	22	0	0 -	-	-	0
Nagaraj	36	0	0 -	-	-	1
Sumathi	31	1	0 -	-	-	0





















PI?	DUR	PI	DRUG	DET	HT	WT	BMI	PR	BP	PULSES
	0 -		AZ/3T/NV			147	50.5	23.27	76 120/80	++
	1		6 TD/3T/NV			157	48.6	19.76	72 110/70	++
	0 -		AZ/3T/NV			142	38.4	19.1	76 116/70	++
	0 -		AZ/3T/NV			170	55	19.03	80 130/90	++
	0 -		D4T/3T/NV			143	43.8	21.47	84 100/66	++
	0 -		AZ/3T/NV			163	55.6	20.98	80 128/74	++
	0 -		AZ/3T/NV			168	62.8	22.16	68 152/100	++
	0 -		AZ/3T/NV			164	51.5	19.2	72 120/72	++
	0 -		AZ/3T/NV			157	58.3	23.69	76 118/80	++
	0 -		AZ/3T/NV			170	74.7	25.8	92 118/68	++
	1		3 TDF/EFV			170	39.1	15.2	92 108/52	PT L +
	0 -		Z/L/E			153	59	25.2	80 90/60	PT B/L +
	1		12 TD/3T/EFV			172	54	18.3	100 150/90	PT B/L +
	0 -		AZ/3T/NV			162	53	20.22	96 90/60	++
	0 -		AZ/3T/NV			170	73	25.26	76 120/70	L PA,PED -
	0 -		ZLN			170	45	15.57	100 90/60	++
	0 -		ZLN			170	65	22.49	80 140/70	++
	0 -		ZLN			154	35	14.76	80 122/70	++
	0 -		ZLN			180	60	18.51	68 130/70	++
	0 -		ZLN			154	63	26.6	88 160/100	++
	0 -		AZT/3T/EFV			148	54	24.7	68 130/70	PT,DP B/L +
	0 -		ZLN			172	72	24.7	76 116/72	++
	0 -		ZLN			157	53	21.54	100 102/60	++
	0 -		SLN			163	46	17.36	80 140/80	++
	0 -		ZLN			170	63	21.8	64 106/60	++
	0 -		ZLN			167	70	25.18	80 140/70	++
	0 -		ZLN			172	49	16.7	78 116/60	++
	0 -		AZ/3T/NV			176	75	24.27	80 120/70	R PT +
	0 -		AZ/3T/NV			166	55	20	80 120/72	++
-	-		-			170	50	17.3	88 124/70	++
	0 -		AZ/3T/NV			158	58	23.29	88 140/80	++
	0 -		AZ/3T/NV			165	73	26.83	76 140/90	++
	0 -		ZLN			152	47	20.34	88 130/70	++
	0 -		ZLN			150	47.9	21.3	84 122/70	++
	0 -		ZLN			154	73	30.8	84 138/82	++
	0 -		SLN			158	76	21.28	76 120/72	++
-	-		-			152	41	17.75	68 128/70	R DP - L DP
-	-		-			168	50	17.73	76 102/60	B/L DP +
	0 -		ZLN			170	55	19.03	68 100/60	++
-	-		-			164	70	26.12	76 140/70	++
	1		4 TLN			152	43	18.69	76 118/68	++
	0 -		ZLN			152	35	15.21	96 124/72	++
	0 -		ZLN			156	40	16.46	68 96/60	++
	0 -		ZLE			172	85	28.81	80 120/70	++
-	-		-			170	45	15.57	120 100/64	++
	0 -		ZLE			175	57	27.66	92 112/74	++
	1		96 NZVRIT			172	47	15.93	76 116/70	++
	1		11 ETENEMTR			176	72	23.3	76 120/70	++
	0 -		TLE			150	53	21.81	94 128/70	PT +

-	-	-	171	44	15.06	80 118/76	++
-	-	-	175	96	31.36	88 148/90	B/L PT +
	0 -	ZLN	170	54	18.69	76 102/60	R DP +
	0 -	ZLE	160	73	28.6	72 120/80	++
	0 -	ZLE	174	69	22.84	80 130/90	++
	0 -	SLN	164	80	29.74	84 110/60	R U&L +,L F
	1	12 TLN	156	82	33.7	78 134/110	L DP&PTA -
	1	7 TLE	152	34	23.4	72 100/80	++
	0 -	ZLN	165	64	23.5	80 122/70	++
	0 -	ZLN	143	57.3	27.9	68 108/70	++
	1	12 TLN	164	43.7	16.2	92 138/84	PA&DP+,P1
	0 -	ZLN	150	47.1	20.9	86 170/110	++
	1	24 TLN	148	45	20.5	78 122/64	++
	0 -	ZLE	170	62.4	23.5	68 128/7	++
	1	7 TLN	153	45.1	19.2	100 138/82	++
	0 -	ZLN	152	46.7	20.2	88 128/78	++
	0 -	ZLN	160	70	27.3	84 152/76	++
	1	12 TLE	153	61.1	26.1	88 152/80	++
	0 -	ZLN	156	70	20.8	76 138/68	++
	1	24 TLE	158	43	17.2	76 122/64	++
	1	12 TLN	150	57.1	25.3	86 98/56	++
	0 -	ZLN	159	65	25.7	72 148/90	++
	1	36 TLN	158	51.9	20.8	86 132/64	B/L PT +
	1	12 TLE	162	57.1	21.7	68 96/50	++
	0 -	ZLE	160	51.2	22.7	58 150/90	++
	0 -	ZLE	170	71.1	24.6	82 112/64	++
	0 -	ZLN	140	64	32.7	78 140/66	++
	0 -	ZLN	164	62	23.1	80 120/64	++
	1	8 TLE	175	62.1	20.2	76 120/70	++
	0 -	ZLN	156	61	25.1	78 118/80	++
	0 -	ZLN	163	48	18.1	96 104/68	++
-	-	-	170	71	24.6	100 140/90	++
	1	1 TRA	168	64	22.7	64 150/90	++
	0 -	ZLN	165	52	19.1	100 140/92	++
	1	4 TLN	172	81.6	27.6	80 120/80	++
	1	4 TLN	172	58.9	19.9	76 160/100	++
	0 -	ZLN	169	69.7	24.5	80 132/80	++
	0 -	ZLN	155	49.1	20.4	78 104/60	++
	0 -	ZLN	170	74	25.6	92 110/70	++
	1	12 TLE	165	60	22.05	76 130/70	++
	0 -	ZLE	164	43.8	16.28	68 108/64	++
-	-	-	152	56	24.24	80 118/60	++
-	-	-	176	68	21.96	76 140/92	++
	1	0.5 TLN	158	40	16.21	92 100/54	++
	1	30 TLE	154	50.5	21.3	96 108/58	++
	0 -	ZLN	156	57.2	23.7	88 140/72	++
-	-	-	170	45	14.38	78 122/80	++
	0 -	ZLN	172	40	13.56	80 100/50	++
-	-	-	164	52	19.33	84 120/80	++
	1	2 TLE	169	49	17.13	76 150/90	++



-	-	-	177	74	23.64	80 126/72	++
-	-	-	180	96	29.63	80 150/82	++
	0 -	ZLE	161	53	20.46	72 104/58	++
-	-	-	158	60	24	88 160/90	++
-	-	-	152	70	30.3	84 152/90	++
	0 -	ZLN	150	50	22.2	86 100/60	++
	0 -	ZLN	176	56	18.12	74 132/80	++
	0 -	ZLE	164	55	20.45	78 110/70	++
	0 -	ZLN	160	63.5	24.8	84 124/70	++
	1	12 TLN	168	86	30.49	88 124/70	++
	0 -	ZLN	166	67	24.36	70 146/68	++
	0 -	ZLE	169	63	22.02	68 128/76	++
	1	6 TLE	171	80	27.39	88 130/90	++
	1	2 TLE	151	43.9	19.25	74 98/50	B/L PTA +
	1	24 TLE	146	34.3	16.1	92 100/50	++
	0 -	ZLN	150	46.9	20.84	76 140/72	++
	0 -	ZLE	155	47.5	19.88	74 116/60	++
	0 -	ZLE	169	65.1	22.84	96 120/76	++
	1	0.26 TLE	152	88.9	38.48	84 142/90	B/L PT&DP
	0 -	ZLN	147	40.5	18.75	82 110/62	++
	1	18 TLE	156	62.5	25.76	76 124/72	++
	1	12 TLE	166	70.6	25.67	84 110/60	++
	0 -	ZLN	164	72.1	26.8	88 142/80	++
	0 -	ZLN	172	78.6	26.64	80 180/100	++
	1	24 TLN	153	41.2	17.6	70 146/68	++
	1	12 TLN	148	49	22.37	72 120/68	++
	0 -	ZLN	172	64	21.69	66 126/70	++
	1	2 TLN	145	40.7	19.38	74 122/60	++
	1	3 TLE	157	57.6	23.41	86 120/72	++
	1	18 TLE	161	59.3	22.89	80 160/80	++
	0 -	ZLN	160	57.2	22.34	84 110/60	++
	0 -	ZLN	168	62.5	22.1	76 128/80	++
-	-	-	175	60	19.6	104 124/82	++
	0 -	ZLN	167	60.7	21.75	68 112/64	++
	0 -	ZLN	168	67.4	26.3	70 130/84	++
	1	12 TLE	164	73	27.13	86 120/70	++
-	-	-	162	90	34.35	72 102/64	++
	1	1 TLE	158	63.9	25.66	76 122/80	++
	1	60 TLN	179	51.8	16.2	80 180/100	++
	1	24 TLN	160	58	20.5	88 124/76	++
	0 -	ZLE	149	36	16.2	72 110/72	++
	0 -	ZLN	165	74.8	27.5	68 142/80	++
	1	4 TLE	174	68.4	22.6	68 128/68	++
	1	6 TLN	152	49	21.2	76 140/90	++
	1	24 TLE	175	61	19.9	74 118/66	++
	0 -	ZLE	158	65.5	26.2	88 104/50	++
	0 -	ZLN	158	46.7	18.7	70 108/70	++
	0 -	ZLE	164	52.8	19.6	72 126/60	++
	0 -	ZLN	168	47	16.7	76 116/58	++
	0 -	ZLN	168	49.8	17.6	78 126/66	++

1	12 TLN	168	77.5	27.5	64 176/98	++
0 -	ZLN	178	72.8	23	78 130/82	++
0 -	ZLN	165	63.5	23.3	74 160/84	++
0 -	ZLN	168	71	25.2	80 118/74	++
0 -	ZLN	153	51	21.8	84 120/70	++
1	5 TLE	158	49.4	19.8	80 126/74	PT,DP +, RL
0 -	ZLE	170	68.6	23.7	80 120/70	++
1	5 TLE	160	55	21.5	74 124/64	++
1	24 TRA	163	57	21.5	90 132/78	++
1	5 TLN	163	71.3	20.8	68 120/68	++
0 -	ZLN	145	47.1	22.4	80 124/66	++
1	18 TLE	168	43.8	15.5	74 126/72	++
0 -	ZLN	166	59.3	21.5	72 110/70	++
0 -	ZLE	170	67.4	23.3	76 138/80	++
1	12 TLN	171	80	27.4	74 154/90	++
1	6 TLN	167	57.9	20.8	80 140/78	++
0 -	ZLN	156	45.4	18.7	68 128/68	++
0 -	ZLN	166	62.9	22.9	80 122/70	++
0 -	ZLN	160	52	20.3	82 142/86	++
0 -	ZLN	165	66	24.3	74 138/72	++
0 -	ZLN	158	56.3	20.1	90 130/68	++
1	30 TLN	145	70.1	25.7	82 138/76	++
1	2 TLE	160	47	18.4	76 102/64	++
1	84 TLN	164	60.7	22	74 130/68	++
0 -	ZLN	168	73.9	26.2	76 140/80	++
1	7 TLN	172	62.5	21.1	64 150/84	++
0 -	ZLE	164	61.5	22.9	78 162/90	++
1	20 TLE	167	66.7	23.9	74 160/100	++
1	24 TRA	173	70	23.4	84 138/76	++
1	3 TLE	150	64.6	28.7	74 126/80	++
0 -	ZLN	166	79.5	28.9	80 162/92	++
0 -	ZLN	158	52.3	21	86 132/70	++
1	24 TLE	148	50	22.8	80 116/70	++
0 -	ZLN	157	40	16.1	68 140/84	++
0 -	ZLN	174	65.8	21.7	84 118/76	++
1	2 TLN	150	39.2	17.4	66 102/58	++
0 -	ZLN	165	49.5	18.4	80 114/72	++
0 -	ZLE	167	62	22.2	76 140/80	++
1	6 TLE	164	56.8	21.1	72 110/68	++
1	24 TLE	172	49.6	16.9	76 120/70	++
0 -	ZLN	163	60	22.6	78 170/100	++
0 -	ZLE	160	62.7	24.5	82 180/98	++
1	12 TLN	173	86	28.7	88 144/80	++
1	7 TLN	164	49	18.2	90 100/68	++
0 -	ZLN	172	72.7	24.6	82 132/78	++
1	24 TLE	165	67.5	24.8	80 156/82	++
1	21 TLE	146	33.5	15.7	96 128/84	++
1	8 TLN	145	45	21.4	80 122/68	++
0 -	ZLN	170	67.4	23.3	78 140/90	++
1	12 TLN	161	46.5	17.9	80 118/76	++

0 -	ZLN	161	49.2	18.9	94 120/64	++
0 -	ZLN	168	70	27.5	80 140/86	++
0 -	ZLN	172	81.4	24.8	76 150/88	++
0 -	ZLN	147	36.9	17.1	66 100/50	++
0 -	ZLE	164	49	18.2	78 130/78	++
1	42 TRA	170	61.2	21.2	84 140/92	++
0 -	ZLE	164	48.8	17.8	74 120/58	++
0 -	ZLN	175	78.2	25.5	76 162/96	++
1	24 TLN	152	58	25.1	82 160/82	++
1	1.5 TLE	171	60	20.5	88 160/88	++
1	14 TLE	157	49	19.9	74 160/80	++
1	48 TLN	158	47.4	18.8	80 124/76	++
1	36 TRA	160	53.3	20.7	74 120/64	++
0 -	ZLE	163	60.4	22.6	76 122/72	++
0 -	ZLE	142	43.8	21.7	82 120/66	B/L PT+
1	24 TLE	169	51.5	17.9	78 110/64	++
0 -	ZLE	168	67.5	23.7	84 176/102	++
0 -	ZLN	158	45.5	18.4	80 136/72	++
0 -	ZLE	157	42.6	17	100 100/56	++
0 -	ZLN	160	59.7	23.4	76 160/90	++
0 -	ZLE	164	46.7	17.5	86 120/74	++
0 -	ZLE	169	60.7	21.4	78 122/70	++
1	60 TLE	163	64.6	24.1	76 140/90	++
1	24 TLE	156	34.4	14.4	94 140/80	++
0 -	ZLE	145	43.9	20.9	86 118/60	++
0 -	ZLN	155	48.2	20	74 138/68	++
0 -	ZLN	154	48	20.2	82 120/60	++
0 -	ZLN	151	69.3	30.7	80 120/68	++
0 -	ZLN	174	79.6	26.4	80 150/80	++
0 -	ZLN	160	72.2	28.1	74 126/78	++
1	3 TLN	147	50.7	23.6	72 110/58	++
1	12 TLN	152	48	20.8	80 120/60	++
0 -	ZLN	166	63.6	23.2	78 160/90	++
1	12 TRA	167	78.5	28.3	80 182/100	++
0 -	ZLE	152	48.7	21.2	76 128/68	++
0 -	ZLN	161	49.8	19.3	82 154/90	++
1	18 TLE	152	72	31.2	78 120/76	++
0 -	ZLN	152	53.3	23.4	76 140/70	++
0 -	ZLN	175	66.5	21.7	76 150/90	++
0 -	ZLN	146	55.5	27.1	86 100/60	++
0 -	ZLN	152	55.5	23.8	84 100/52	++
0 -	ZLN	169	58.7	20.2	68 160/90	++
0 -	ZLN	164	57.3	21.6	80 124/72	++
0 -	ZLE	159	48.1	19	76 122/70	++
0 -	ZLN	160	60.2	23.4	78 142/80	++
1	12 TLN	151	41.7	18	74 110/70	++
0 -	ZLE	154	59.8	25.3	72 162/80	++
0 -	ZLE	163	61.9	23.3	72 150/80	R-PT/DP+,L
-	-	162	63	24	84 150/92	++
0 -	ZLE	156	55.2	22.6	80 112/64	++

0 -	ZLN	168	68	23.8	80 144/76	++
1	24 TLN	170	88.4	30.8	74 126/78	++
0 -	ZLE	165	46	16.9	72 100/58	++
0 -	ZLN	154	50	21.1	76 116/66	++
0 -	ZLN	171	75.5	26	76 126/70	++
0 -	ZLN	153	40	17.1	74 130/70	++
1	7 TRA	168	75	26.6	88 110/68	++
0 -	ZLN	156	50	20.5	64 126/70	++
1	18 TLE	170	67.1	23.2	86 130/70	++
0 -	ZLN	184	70.6	21	74 124/76	++
0 -	ZLN	156	48.3	20.1	76 120/70	++
0 -	ZLN	156	51.6	21.4	78 124/76	++
1	24 TLN	165	47.2	17.6	84 120/78	++
0 -	ZLN	159	73	28.9	74 148/82	++
0 -	ZLN	175	82	26.8	76 142/90	++
0 -	ZLN	179	72.9	22.8	96 122/68	++
0 -	ZLN	177	66.7	21.4	76 140/80	++
1	12 TLN	165	53.2	19.5	86 162/80	++
0 -	ZLN	164	57.8	21.6	78 140/82	++
1	22 TLE	152	57.5	25.1	68 112/58	++
0 -	ZLE	159	56.2	22.2	80 140/86	++
0 -	ZLN	170	65	22.5	80 160/88	++
0 -	ZLE	169	59	20.7	76 130/70	L-PT&DP -,I
1	3 TLE	174	82	27.1	74 120/90	++
1	0.5 TLE	154	41.9	17.7	88 104/60	++
0 -	ZLN	160	53.2	20.7	68 116/72	++
0 -	ZLN	145	60.3	28.7	78 110/72	++
0 -	ZLN	172	48	16.2	78 112/68	++
0 -	ZLN	170	71	24.6	80 120/70	++
1	14 TLN	148	47.1	21.5	74 122/64	++
0 -	ZLN	140	52	26.5	76 112/66	++
0 -	ZLN	154	53	22.3	80 130/76	++
0 -	ZLN	170	59.1	2.04	78 130/80	++
0 -	ZLN	150	56	24.9	92 120/70	++
0 -	ZLN	150	42.7	19	86 90/58	++
0 -	ZLN	164	64.2	23.1	80 140/82	++
0 -	ZLN	155	54	22.5	76 136/74	++
0 -	ZLN	162	45	17.1	74 96/66	++
0 -	ZLN	174	73	24.1	94 134/80	++
1	6 TLN	159	48.1	19	64 120/74	++
1	3 TLE	150	55.1	24.5	84 120/62	++
1	18 TLE	156	40.3	16.6	80 120/76	++
0 -	ZLN	168	82.6	29.3	100 146/86	++
0 -	ZLN	156	59.6	24.6	84 150/74	++
0 -	ZLN	156	54	22.2	88 190/100	++
0 -	ZLE	140	43	21.9	74 130/90	++
0 -	ZLN	168	41.1	14.6	76 118/64	++
-	-	152	54	23.9	78 110/58	++
1	12 TLN	158	51	20.4	86 120/80	++
1	3 TLE	150	45.9	20.4	80 130/80	++

1	2 TLE	159	49.1	19.4	74 120/64	B/LU+,L;DP
0 -	ZLN	174	67	22.1	76 106/58	++
0 -	ZLN	162	46.3	17.6	80 120/80	++
0 -	ZLN	172	75.2	25.4	82 152/88	++
0 -	ZLN	150	34.1	15.2	80 102/60	++
-	-	172	65	22	74 102/72	++
-	-	158	53	21.2	76 142/90	++
1	1 TLE	166	46.8	17	76 102/62	++
1	0.5 TLE	169	56.9	19.9	80 150/90	++
0 -	ZLN	149	53.2	24	76 142/84	++
0 -	ZLN	157	53	21.5	68 122/68	++
0 -	ZLN	136	27.4	14.8	94 100/54	++
0 -	ZLN	162	63	24	74 130/82	++
0 -	ZLE	162	51.4	19.6	76 90/50	++
0 -	ZLN	163	58.7	22.1	78 126/74	++
0 -	ZLN	147	60.3	27.9	66 112/54	++
0 -	ZLN	171	46.2	15.2	78 140/70	++
1	16 TLE	148	61.1	27.9	80 150/80	++
1	24 TAR	148	39	17.8	76 96/52	++
1	24 TRA	160	38	14.8	84 110/70	++
0 -	ZLN	148	56	25.6	80 120/72	++
0 -	ZLE	156	45.6	18.7	74 130/76	++
0 -	ZLN	162	50	19.1	76 130/72	++
1	21 TLN	164	57.3	21.3	74 120/100	++
0 -	ZLN	176	77	24.9	88 130/78	++
0 -	ZLN	161	61.3	23.6	84 136/74	++
0 -	ZL	160	65.9	25.7	74 128/68	++
0 -	ZLN	160	51.6	20.2	76 124/72	++
0 -	ZLN	150	39	17.3	78 126/66	++
0 -	ZLN	164	59.9	22.3	82 120/74	++
0 -	ZLN	160	63.8	24.9	68 140/90	++
0 -	ZLN	159	48	19	84 140/86	++
1	5 TLE	146	44.6	20.9	72 120/70	L-PT&DP+
1	6 TLN	154	45	19	88 140/84	DP+
0 -	ZLN	160	50.8	23.4	86 110/70	PT,DPB/L -,
0 -	ZLN	156	78	32.1	84 120/72	++
0 -	ZLN	150	56	24.9	72 110/64	++
0 -	ZLN	169	57.4	20.1	80 120/80	++
1	8 TLN	170	54.4	18.8	76 128/72	++
0 -	ZLE	164	37.6	14	78 90/62	++
0 -	ZLN	165	60	22	74 130/70	++
0 -	ZLN	157	54.8	22.2	90 126/74	++
1	12 TLN	142	39.8	19.7	80 122/70	++
1	20 TLN	170	76.2	26.4	84 132/74	++
0 -	ZLN	153	46.9	20	78 116/58	++
0 -	ZLN	148	57.5	26.3	92 124/68	++
0 -	ZLN	150	52.9	23.5	68 130/80	++
0 -	ZLE	174	59	19.5	74 118/56	++
0 -	ZLN	176	65.9	21.3	80 118/60	++
0 -	ZLE	152	46.5	20.1	76 124/66	++

0 -	ZLN	140	61.7	31.5	78 156/76	++
0 -	ZLN	148	39.5	18	80 100/58	++
0 -	ZLN	168	55.3	19.6	72 120/76	++
0 -	ZLN	170	64	22.1	78 130/66	++
0 -	ZLN	167	65.7	23.6	80 128/64	++
0 -	ZLN	153	46	19.7	74 96/54	++
1	36 TLN	155	44.6	18.4	80 110/68	++
0 -	ZLN	150	51.7	23	76 110/78	++
0 -	ZLN	166	61.2	22.2	86 130/88	++
0 -	ZLN	166	101	36.4	72 120/80	++
0 -	ZLN	164	46.4	17.3	80 90/60	++
1	4 TLN	160	70.9	27.7	72 110/60	++
1	48 TLE	159	54	21.4	76 100/58	++
0 -	ZLN	176	82	26.2	74 130/72	++
0 -	ZLN	167	58	20.9	76 170/100	++
1	24 TLN	157	66.3	26.9	84 124/72	++
0 -	ZLN	170	70.7	24.5	80 120/70	++
0 -	ZLN	145	42.7	20.3	66 100/52	++
0 -	ZLN	155	65.8	27.4	72 110/58	++
0 -	ZLN	169	58	20.3	76 130/70	++
0 -	ZLN	170	64	22.1	78 116/68	++
0 -	ZLN	144	58.8	28.4	70 110/70	++
0 -	ZLN	155	52.2	21.7	78 110/60	++
0 -	ZLN	157	64.6	26.2	88 100/52	++
0 -	ZLN	164	55.1	20.5	80 118/68	++
0 -	ZLN	148	42.8	19.5	70 118/72	++
0 -	ZLN	163	57.3	21.7	64 122/72	++
1	7 TLN	172	86	29.1	86 130/80	++
0 -	ZLN	175	49.8	16.3	76 134/80	++
0 -	ZLN	160	59.2	23.1	88 100/64	++
0 -	ZLN	165	68.6	25.2	84 130/80	++
0 -	ZLN	170	69.4	24	78 140/72	++
0 -	ZLN	157	56	22.7	100 116/62	++
1	12 TLE	172	63	21.3	76 130/78	++
0 -	ZLN	154	60.6	25.6	90 118/58	++
0 -	ZLN	154	53.2	27.5	68 114/74	++
0 -	ZLN	152	60.3	26.1	76 110/70	++
1	48 TLN	155	57	23.7	84 110/66	++
1	8 TLN	164	48.8	18.1	88 116/70	++
0 -	ZLN	170	49.1	17	84 90/54	++
1	18 TLN	176	82.5	26.6	72 160/100	++
0 -	ZLN	167	58.6	21	78 110/58	++
0 -	ZLE	155	61.8	25.7	76 128/70	++
1	42 TAR	168	61.5	21.8	76 128/80	++
1	3 TLE	164	53	19.7	96 130/76	++
0 -	ZLN	166	67.9	24.6	84 130/74	++
1	84 TLE	152	54.6	23.6	96 124/70	++
1	12 TLE	154	67.7	28.5	84 132/80	++
0 -	ZLN	153	55	23.5	76 140/80	++
0 -	ZLN	165	62	22.8	100 108/58	++

0 -	ZLN	156	46.1	18.9	92 116/54	++
1	26 TLN	154	52	21.9	80 108/62	++
0 -	ZLN	159	53.4	21.1	76 124/74	++
0 -	ZLE	149	46.4	20.9	76 120/72	++

ABI Re-R	ABI Re-L	ABPI Ex-R	ABPI Ex-L	TP-R	TP-L	HB	T.CHOLEST	TG	
1.08	1	0.91	1.08	-	-		12.2	281	494
0.96	0.98	1.05	1.07	-	-		12.8	N/A	
0.91	0.91	0.91	0.9	-	-		12	N/A	
1.04	1	1	1	-	-		12	190	108
1.2	1.18	1.06	1.04	100	90		13.3	N/A	
1.11	1.12	0.97	1.01	141	140		14.9	115	130
1.27	1.31	1.14	1.11	134	164		14.3	204	232
0.98	0.96	1.03	0.94	-	-		13.9	N/A	
1.1	1.15	1.2	1.32	118	72		13.1	N/A	
1.08	1.2	1.21	1.14	118	120		14.3	165	94
1.03	1	0.98	0.85	-	-		9.2	N/A	
0.9	1.33	0.9	1.22	80	40		12.2	N/A	
1.2	1.13	0.94	0.88	110	94		12.6	188	86
1	1	1.11	0.88	-	-		8.1	N/A	
1.42	0.32	1	0.3	100	0		14.6	117	148
1.11	1.11	1	1	-	-		9.9	N/A	
1	1.14	1.14	1	70	88		12.9	270	231
1.23	1.14	1.06	1.14	80	84		9.1	N/A	
0.92	0.95	0.87	0.87	-	-		13.9	N/A	
1.12	1	1.09	0.96	-	-		12.7	162	139
1.01	0.91	0.95	0.88	-	-		13.2	N/A	
1.12	1.1	1.06	1.11	-	-		13.8	127	94
1.07	1.03	1.02	1	-	-		12	150	88
1	0.94	0.98	0.95	-	-		8.1	162	160
1.03	1.09	1.07	1.07	-	-		12.3	N/A	
1	0.95	0.98	0.9	-	-		12.5	N/A	
0.98	0.95	0.93	0.93	-	-		14.4	N/A	
1.03	1.12	1	1.02	-	-		11.4	236	218
1	1.08	0.98	0.96	-	-		9.4	N/A	
0.92	1	0.9	0.96	-	-		14	N/A	
1	1	0.96	0.94	-	-		14.8	N/A	
1.06	1.1	0.99	0.98	-	-		15.2	105	266
1.07	1.09	1	1.04	-	-		13.4	87	94
1.05	1.02	1.03	1	-	-		10.1	N/A	
0.94	1.09	0.95	0.95	-	-		13.5	N/A	
1.08	1.1	1	1.02	-	-		12.6	210	247
0.91	1.03	0.88	0.95	-	-		11.1	N/A	
1	1.07	0.99	1.03	-	-		13	N/A	
1.02	1.04	1	0.96	-	-		9	N/A	
1.04	1.02	0.97	0.98	-	-		9.3	136	161
1	1.01	0.96	0.95	-	-		12.4	134	124
0.94	0.96	0.91	0.92	-	-		10.7	N/A	
1.16	1.96	1.1	1.8	80	70		9.9	N/A	
0.95	1.11	0.92	1.05	-	-		14.6	N/A	
0.96	1.1	0.91	0.97	-	-		5.7	N/A	
1.09	1.07	1.01	1.02	-	-		10.6	N/A	
1.02	1	1.02	0.97	-	-		13.2	N/A	
1.06	1.08	1.01	1.02	-	-		14.5	N/A	
0.93	0.95	0.9	0.93	-	-		9.4	N/A	



1.02	1.08	0.97	0.99 -	-		9.3	150	104
1.01	1.08	0.96	1 -	-		14.1	167	208
1.07	0.94	1.06	0.92 -	-		13.7 N/A	N/A	
1.07	1.1	1.08	1.07 -	-		11.6 N/A	N/A	
1.05	1.03	1	1.04 -	-		10.6 N/A	N/A	
1.07	1.09	1.06	1 -	-		14.5 N/A	N/A	
0.93	0.84	0.84	0.81 -	-		11.4 N/A	N/A	
1	1.22	1.2	1.18	90	110	9.2 N/A	N/A	
1.14	1.08	1.25	1.17	108	112	14.2	173	119
1.15	1.09	1.03	1.07 -	-		11.5 N/A	N/A	
0.89	0.86	0.89	0.95 -	-		12.6 N/A	N/A	
1.07	1.06	1.04	1.04 -	-		11.5	166	76
1.07	1.08	1.09	1.03 -	-		10.9	182	129
0.95	0.97	1	1.05 -	-		11.1	120	119
1.03	1.03	1.13	1.06 -	-		9.5 N/A	N/A	
0.97	0.92	0.94	0.92 -	-		12.1 N/A	N/A	
1.05	0.99	0.98	1 -	-		14.1 N/A	N/A	
1.07	0.97	1.05	0.83 -	-		12.5	192	167
0.91	0.91	1.06	1 -	-		11.3	162	128
1.15	1.07	1.08	1.2	100	98	11.6	153	236
1.14	1.31	1.04	1.07	104	114	12.2 N/A	N/A	
1	0.93	1.11	1.01 -	-		11.9 N/A	N/A	
1.06	0.98	0.86	0.81 -	-		13 N/A	N/A	
1.12	1.25	1.11	1.09	108	120	14.7	151	128
1.01	1.05	1.01	1.03 -	-		11.3	136	77
1.07	1.09	1.02	1.1 -	-		13.1 N/A	N/A	
1.14	1.14	1.12	1.07	104	102	15.3	181	283
1.03	1.08	0.98	0.97 -	-		12.8 N/A	N/A	
1.02	1.03	1.12	1.04	100	88	13.6 N/A	N/A	
1.05	1.08	1.03	1.05 -	-		10.1 N/A	N/A	
1	1.08	0.92	0.98 -	-		9	118	248
1.06	1.07	1	1.01 -	-		16.5 N/A	N/A	
1.07	1.07	1.03	1.03 -	-		11.7	160	133
1.14	1.07	1.04	1.03	88	102	14.7 N/A	N/A	
1.07	1.03	1.03	1.05 -	-		13.8	112	58
1.02	1	1.01	0.98 -	-		12.2 N/A	N/A	
1.02	0.98	1.03	1.06 -	-		13.5	136	94
1.06	1.02	0.93	1 -	-		11.9 N/A	N/A	
1.09	0.98	0.98	0.92 -	-		11.4	179	120
0.96	0.91	0.94	0.91 -	-		9.4 N/A	N/A	
1.04	1	1.05	0.98 -	-		11.7 N/A	N/A	
0.92	0.92	0.92	0.91 -	-		10.2 N/A	N/A	
0.99	0.93	0.91	1 -	-		11.4	120	426
1.1	1.08	1	1.04 -	-		8.7	170	134
1.07	1	1.02	0.98 -	-		9.9 N/A	N/A	
1.21	1.16	1.19	1.1	110	102	11.5	139	482
0.98	1.02	0.91	0.91 -	-		10.6 N/A	N/A	
1.02	1	1.01	0.98 -	-		15.6 N/A	N/A	
1.17	1.03	1.02	1.03 -	-		9.7 N/A	N/A	
1.06	1.05	1.14	0.97 -	-		12.5 N/A	N/A	

0.98	1.02	0.98	0.98	-	-	15.5	158	158
1.01	1.07	1.13	0.99	-	-	15.7	113	154
1.04	1	0.97	1.01	-	-	11.8	N/A	N/A
0.97	0.93	1.08	1.09	-	-	10.5	N/A	N/A
1.18	1.13	1.07	1.1	98	114	13.6	N/A	N/A
1.06	1.02	0.98	1	-	-	11.4	203	237
0.94	0.95	1.15	1.12	-	-	13.2	171	457
0.91	0.91	0.93	0.91	-	-	11.8	N/A	N/A
1	1.13	1.02	1.1	-	-	14.6	N/A	N/A
1.15	1.16	1.18	1.05	88	96	12.8	146	201
1.04	1.15	1.05	1.15	118	104	15.7	N/A	N/A
1	0.98	1.03	1.02	-	-	11.5	N/A	N/A
1.09	1.15	1.12	1.15	-	-	13.5	N/A	N/A
0.89	0.87	0.88	0.9	-	-	12.1	N/A	N/A
1.08	1.1	1.02	1	-	-	12.6	N/A	N/A
0.97	0.93	1.05	1.02	-	-	12.7	N/A	N/A
1.01	1.03	1	1.03	-	-	11.7	N/A	N/A
1.01	1	1.16	1.13	-	-	12.9	N/A	N/A
0.87	1.01	0.97	0.97	-	-	10	N/A	N/A
0.98	0.98	0.95	0.93	-	-	11.4	N/A	N/A
1	1.01	0.91	1	-	-	10.6	N/A	N/A
1.09	1	1	0.98	-	-	10.6	N/A	N/A
1.05	1	1.02	1.1	-	-	15.2	105	266
1.13	1.04	1.13	1	-	-	15.8	185	165
1.01	1.02	0.97	1.02	-	-	14.8	N/A	N/A
1	0.98	1.04	0.98	-	-	10.2	138	167
1	1.03	1.04	1.07	-	-	15.2	137	120
1.02	0.98	1.07	1.09	-	-	9.8	N/A	N/A
1.02	1	1	1.08	-	-	11.9	N/A	N/A
1.01	1	0.98	0.93	-	-	8	N/A	N/A
1.09	1.09	1.02	1.02	-	-	12	102	255
1.03	0.94	1.03	1.02	-	-	14.9	N/A	N/A
1.13	1.15	1.04	1.07	-	-	6.8	124	181
1.02	1.08	1	0.98	-	-	14.8	N/A	N/A
1	1	1.02	1	-	-	14.9	167	168
1	0.98	1.03	1.08	-	-	15	N/A	N/A
0.98	0.94	1.08	0.96	-	-	15.9	N/A	N/A
1.08	1.11	1.07	1.08	-	-	13.5	N/A	N/A
0.94	0.9	0.98	0.97	-	-	14.8	N/A	N/A
0.97	0.94	0.92	0.92	-	-	13.2	N/A	N/A
0.91	0.95	0.92	0.92	-	-	10.2	N/A	N/A
0.92	0.93	0.91	0.93	-	-	16	N/A	N/A
1.03	1.02	0.92	0.92	-	-	10.7	116	92
1.01	1.04	0.93	0.95	-	-	12	N/A	N/A
0.92	0.93	0.93	0.95	-	-	13.1	N/A	N/A
0.96	1.04	0.96	0.98	-	-	11.5	N/A	N/A
1.02	1.04	0.98	1.02	-	-	15.1	135	56
0.95	0.97	0.95	0.83	-	-	13.5	N/A	N/A
0.95	1.03	1.08	1.1	-	-	15.3	N/A	N/A
0.95	0.98	0.98	0.93	-	-	14.7	N/A	N/A

0.98	1.03	1.1	0.96	-	-	16.8	N/A	N/A
1.02	1.08	1.06	1.04	-	-	14.3	109	194
1.01	1	0.97	0.94	-	-	13.1	201	178
1.02	0.98	0.95	0.92	-	-	12.3	N/A	N/A
0.98	0.93	0.94	0.92	-	-	11.1	101	88
0.89	0.87	0.86	0.83	-	-	14	N/A	N/A
1.02	1	0.98	1.05	-	-	13.9	N/A	N/A
1.03	1.05	0.97	0.98	-	-	14	N/A	N/A
0.93	0.94	1.03	1.01	-	-	15.3	N/A	N/A
0.97	0.92	0.97	0.92	-	-	6.4	N/A	N/A
0.97	1	0.94	0.95	-	-	13.4	N/A	N/A
1.03	1.02	1.01	0.99	-	-	14.6	N/A	N/A
1.09	1.07	0.98	0.98	-	-	13.4	N/A	N/A
1.01	0.99	1.01	0.99	-	-	13.3	145	176
0.97	1.1	1.07	1.13	-	-	14.5	202	233
1.09	1.07	1.07	1.08	-	-	12	N/A	N/A
0.94	0.92	0.94	0.9	-	-	12.3	N/A	N/A
1.08	1.03	1.1	1.09	-	-	15.3	N/A	N/A
1.13	1.2	1.21	1.15	94	120	12.5	348	1385
0.99	1.03	0.99	0.99	-	-	12	N/A	N/A
1.06	1.12	0.99	0.97	-	-	13.8	144	80
1.06	1.07	1.01	0.94	-	-	15.6	N/A	N/A
0.98	1.08	0.95	0.93	-	-	10.1	N/A	N/A
1	1.02	0.99	0.97	-	-	14.3	N/A	N/A
1.01	0.96	1.06	1.01	-	-	13.4	N/A	N/A
0.95	0.93	0.92	0.94	-	-	13.8	162	106
0.99	0.96	0.92	0.93	-	-	13.5	N/A	N/A
0.93	0.99	0.9	0.96	-	-	12.1	N/A	N/A
1.04	1.12	0.99	1.03	-	-	13	N/A	N/A
0.92	0.9	0.89	0.9	-	-	12.3	N/A	N/A
1.06	1.1	0.99	1.01	-	-	12.3	160	123
1.06	1.12	0.96	0.94	-	-	12.4	N/A	N/A
0.95	0.95	0.92	0.91	-	-	8.9	N/A	N/A
1.07	1.14	1.03	1.04	-	-	11	230	865
0.92	0.98	0.97	0.98	-	-	15	174	102
1.06	0.94	1	1.04	-	-	14.2	N/A	N/A
0.87	0.89	0.95	1	-	-	12.7	N/A	N/A
0.94	0.93	0.96	0.96	-	-	12.2	N/A	N/A
0.91	0.9	0.9	0.96	-	-	8.5	222	89
0.92	0.95	1.07	0.91	-	-	15.9	136	143
1.06	1.14	1.1	1.05	-	-	13.2	N/A	N/A
1.02	1	1.01	1.04	-	-	15.1	194	263
1.25	1.15	1.12	1.1	80	90	10.9	176	87
0.98	1.04	0.96	0.98	-	-	7.8	N/A	N/A
1.06	1.08	1.09	1.09	-	-	13.8	N/A	N/A
0.91	0.94	0.95	0.96	-	-	14	N/A	N/A
0.92	0.91	0.89	0.87	-	-	9.4	N/A	N/A
0.98	0.97	0.98	0.95	-	-	14.5	171	97
1.01	1.03	1.02	1	-	-	15.6	N/A	N/A
1.03	1	0.93	0.95	-	-	9.7	N/A	N/A

0.9	0.92	0.98	0.92 -	-		12.4	N/A	N/A
1.01	1	0.99	0.99 -	-		12.5	N/A	N/A
0.99	0.95	0.87	0.91 -	-		15.5	N/A	N/A
1.1	0.98	0.96	0.94 -	-		11	N/A	N/A
0.98	0.94	0.92	0.9 -	-		12.6	N/A	N/A
1.07	1.06	1.08	1.07 -	-		17.4	N/A	N/A
1.02	0.92	0.91	0.92 -	-		11.1	N/A	N/A
1.01	0.99	0.95	0.93 -	-		13.6	N/A	N/A
1.01	1.02	0.98	0.99 -	-		13	N/A	N/A
1.06	1.05	1.01	0.99 -	-		16.4	N/A	N/A
0.93	0.94	0.97	0.99 -	-		10.4	N/A	N/A
1.21	1.25	1.21	1.29	84	72	12.3	N/A	N/A
1	0.98	0.98	0.95 -	-		9.8	N/A	N/A
0.91	0.97	0.91	0.92 -	-		13.5	N/A	N/A
1.02	0.95	0.98	1.01 -	-		10.7	N/A	N/A
0.91	0.91	1	0.98 -	-		7.9	N/A	N/A
0.97	0.97	0.94	0.93 -	-		15.5	218	373
0.99	1.01	0.97	1 -	-		10.6	164	94
0.9	0.98	0.98	0.96 -	-		11.9	156	60
1.01	0.99	1.02	1.01 -	-		17	141	81
0.9	0.93	0.98	0.97 -	-		10.5	N/A	N/A
1.14	0.92	0.95	0.97 -	-		10.3	N/A	N/A
1.01	1	0.99	0.99 -	-		13.1	N/A	N/A
0.9	0.91	0.94	0.91 -	-		10.8	N/A	N/A
1.02	0.95	1.05	1.02 -	-		11	N/A	N/A
0.96	0.99	0.94	0.96 -	-		12.4	N/A	N/A
1.02	1	0.98	1 -	-		12.6	N/A	N/A
1.02	0.98	0.92	0.96 -	-		13.3	N/A	N/A
1.07	1.08	0.99	1.02 -	-		14.1	N/A	N/A
1.11	1.19	1.07	1.09	100	110	11.6	N/A	N/A
0.96	1	0.94	0.98 -	-		10.8	N/A	N/A
1	1.1	0.97	1 -	-		13.8	N/A	N/A
1.13	1.11	1.12	1.05 -	-		13.5	N/A	N/A
1.09	1.04	1.01	1.02 -	-		14.3	211	100
0.94	0.97	0.98	0.96 -	-		14.6	147	76
0.97	0.92	0.94	0.96 -	-		13.3	229	242
1.02	1.03	0.98	1 -	-		12.1	161	341
1.03	1.01	1.06	1.09 -	-		11.7	N/A	N/A
1.2	1.17	1.08	1.08	100	108	13.2	N/A	N/A
1.02	0.98	0.92	0.94 -	-		14	N/A	N/A
0.96	1.02	0.94	0.96 -	-		12.2	N/A	N/A
0.91	0.93	0.9	0.92 -	-		12.1	146	307
1.09	1.11	1.06	1.09 -	-		12.6	N/A	N/A
1.07	1.08	1.07	1.11 -	-		12.5	N/A	N/A
1.13	1.06	1.04	0.94 -	-		15.3	N/A	N/A
0.87	0.89	0.91	0.87 -	-		12.4	134	124
0.94	0.94	0.93	0.93 -	-		13.6	N/A	N/A
0.85	0.87	0.91	0.89 -	-		14.2	N/A	N/A
1.06	1.08	1.04	1.06 -	-		14.2	N/A	N/A
0.9	0.91	0.91	0.9 -	-		12.6	N/A	N/A

0.99	1.03	1.07	1.08	-	-	12.6	N/A	N/A
1.11	1.13	1.21	1.1	100	90	14.3	N/A	N/A
1.02	1.04	1	1.02	-	-	10.5	N/A	N/A
1.03	0.95	1.02	1	-	-	6.6	N/A	N/A
1.07	1.05	1.06	1.05	-	-	16.7	N/A	N/A
1	1.05	0.98	0.98	-	-	13.1	N/A	N/A
1.13	1.05	1.12	1.03	-	-	14.5	N/A	N/A
0.98	0.97	1.03	0.98	-	-	12.7	N/A	N/A
1.05	0.98	0.98	0.98	-	-	11.3	N/A	N/A
0.94	0.97	0.94	0.92	-	-	14.2	N/A	N/A
1.03	1.02	0.99	0.98	-	-	12.1	N/A	N/A
1.02	0.98	1.03	1.02	-	-	9.8	N/A	N/A
1	0.97	1.1	1.09	-	-	12	156	102
1.22	1.2	1.09	1.22	190	150	12.8	201	579
1.06	1.27	1.17	1.21	140	124	14.6	192	280
1.02	1.08	1	1.04	-	-	15	N/A	N/A
1.01	1.04	1.01	1	-	-	12.4	N/A	N/A
1.01	1.02	0.99	0.97	-	-	15	N/A	N/A
1.01	1.07	0.96	0.99	-	-	13.6	N/A	N/A
0.91	0.95	1.03	1	-	-	11.2	N/A	N/A
0.91	0.93	0.97	0.94	-	-	11.3	N/A	N/A
1.05	1.06	1.01	1	-	-	14.2	151	170
0.92	0.85	0.98	0.77	-	-	13	N/A	N/A
1.02	0.98	1.11	1.03	-	-	13.8	N/A	N/A
1.04	1.04	0.91	1.02	-	-	11.4	N/A	N/A
1.09	1.12	0.98	1.07	-	-	10.5	99	154
0.98	1.02	0.93	1.02	-	-	12.1	N/A	N/A
0.96	0.95	1.03	0.95	-	-	6.6	N/A	N/A
1.08	1	0.95	1.11	-	-	6.5	257	1163
0.98	1.07	0.92	0.95	-	-	12.4	N/A	N/A
0.93	0.91	1	0.97	-	-	12.1	175	118
1.15	1.08	1.02	0.97	-	-	14.1	N/A	N/A
1.08	1.08	0.95	0.97	-	-	11.2	N/A	N/A
0.98	1.03	1.07	1	-	-	10.1	N/A	N/A
1.22	1.11	1.1	1.08	110	100	11.8	N/A	N/A
1.06	0.99	1.04	1.01	-	-	12.4	N/A	N/A
1.07	1.1	1.11	1.14	-	-	13.6	N/A	N/A
1.12	1.04	1.2	1.16	90	80	11.9	N/A	N/A
1.09	1.03	1.06	1.03	-	-	15.1	131	N/A
1.03	1.07	1.11	1.07	-	-	14.2	N/A	N/A
1.03	1.07	1.07	1.02	-	-	12.8	N/A	N/A
0.92	0.9	0.95	0.93	-	-	12.9	N/A	N/A
0.88	0.86	0.96	0.88	-	-	11.1	N/A	N/A
0.93	1.07	0.95	0.96	-	-	10.7	N/A	N/A
1.11	1.03	1.03	0.99	-	-	13.4	N/A	N/A
1.03	0.98	1.02	0.98	-	-	12.1	198	104
0.92	0.95	0.94	0.92	-	-	12.3	N/A	N/A
1.02	0.98	0.98	0.95	-	-	11.8	N/A	N/A
0.92	1.03	0.92	0.91	-	-	11.2	N/A	N/A
0.95	0.91	0.94	0.97	-	-	14.1	N/A	N/A

0.83	0.85	0.9	0.8	-	-	8.5	200	110
1.13	1.13	1.07	1.02	-	-	14.7 N/A	N/A	
0.91	0.91	0.94	0.98	-	-	9.4 N/A	N/A	
1.18	1.24	1.13	1.19	84	96	11.1 N/A	N/A	
0.98	1	1.02	0.98	-	-	11.6 N/A	N/A	
0.98	1.07	1	0.96	-	-	12.7 N/A	N/A	
1	0.98	1.01	0.98	-	-	11.3	112	212
0.98	1.05	0.81	0.96	-	-	10 N/A	N/A	
0.6	0.61	0.64	0.63	-	-	12.8 N/A	N/A	
1.13	1.14	1.09	1.11	-	-	12.9	260	1100
1.01	1.06	0.96	1.01	-	-	11 N/A	N/A	
0.96	0.99	0.97	0.9	-	-	9.5 N/A	N/A	
1.23	1.11	1.21	1.05	82	90	5.7	88	102
1.02	1	0.98	0.99	-	-	12.2 N/A	N/A	
1.01	1.04	0.97	0.98	-	-	12.6	184	100
1.05	0.98	1.01	0.96	-	-	12.8 N/A	N/A	
0.94	0.92	0.92	0.94	-	-	16.2 N/A	N/A	
1.05	1.06	1.05	0.97	-	-	12.7 N/A	N/A	
1.1	1.14	1.14	1.04	-	-	12.5	192	82
1.07	1.05	1.03	1.01	-	-	14.8 N/A	N/A	
1.03	1.06	1.03	1.06	-	-	11.2	144	70
0.96	0.92	1.01	0.95	-	-	14.3 N/A	N/A	
0.96	0.9	1	0.93	-	-	13.5 N/A	N/A	
1.03	0.91	1.01	0.91	-	-	14.3 N/A	N/A	
1.06	1.07	1.06	1.06	-	-	13.3 N/A	N/A	
1.04	1.07	1.19	1.06	100	114	14.8 N/A	N/A	
1.07	1	0.98	0.93	-	-	13.3 N/A	N/A	
1.01	1.04	1	0.98	-	-	11.8 N/A	N/A	
0.88	0.9	0.96	0.94	-	-	14.5	184	102
1.08	1.13	1.15	1.07	-	-	12.8 N/A	N/A	
1.27	1.32	1.08	1.19	104	90	13.4 N/A	N/A	
1.05	1.01	1.04	1.07	-	-	10.9 N/A	N/A	
1.08	1.01	0.95	0.79	-	-	11.3 N/A	N/A	
1.25	1.24	1.13	1.07	100	90	11.3 N/A	N/A	
0.27	0.36	0.3	0.3	-	-	14	240	108
1	1.08	1.08	1.07	-	-	13.8 N/A	N/A	
1	1.09	11.01	1.05	-	-	10.2 N/A	N/A	
1.1	1	1.14	1.12	-	-	14.7 N/A	N/A	
1.06	1.08	1.09	1.12	-	-	14.7 N/A	N/A	
1	1	1.1	1	-	-	11.6 N/A	N/A	
0.98	1.08	1.13	1.08	-	-	12.1 N/A	N/A	
0.96	1.01	1.27	1.23	124	110	13 N/A	N/A	
1.01	1.06	0.9	0.93	-	-	7.5 N/A	N/A	
0.98	1.01	0.91	0.94	-	-	15.8 N/A	N/A	
0.94	0.96	1.07	0.98	-	-	12.7 N/A	N/A	
0.98	1.08	1.06	1.03	-	-	13.9 N/A	N/A	
1.01	1	0.98	0.92	-	-	12.5 N/A	N/A	
0.98	1.05	1.01	1.1	-	-	12.7 N/A	N/A	
1.1	1.03	0.93	0.91	-	-	13.8 N/A	N/A	
1.03	1.04	0.94	0.98	-	-	11.3 N/A	N/A	

1.03	1.02	0.95	0.92	-	-	12.2	N/A	N/A	
1.04	1.06	1.09	0.96	-	-	14	N/A	N/A	
1.08	1.1	1.03	1.04	-	-	13.8		184	92
1.07	1.03	0.97	0.92	-	-	N/A	N/A	N/A	
1.01	1.04	1.04	1.04	-	-	14.7	N/A	N/A	
1.08	1.12	1.08	1.06	-	-	12.6	N/A	N/A	
1.09	1.07	1.03	0.98	-	-	10.2	N/A	N/A	
0.96	0.98	1.01	1.03	-	-	10.4	N/A	N/A	
1.06	1.04	1.01	1.03	-	-	14.5	N/A	N/A	
1.14	1.1	1.12	1.03	-	-	14.6	N/A	N/A	
1.2	1.31	1.16	1.18		90 100	11.5	N/A	N/A	
1.1	1.05	1.07	1.01	-	-	12.7		126	87
1.04	1	0.92	1	-	-	16.2	N/A	N/A	
1.09	1.07	1.07	1.02	-	-	13.3		185	244
0.94	0.92	0.92	0.95	-	-	9.9	N/A	N/A	
1.03	1.06	1.01	1.09	-	-	11.6	N/A	N/A	
0.91	0.98	0.95	1.03	-	-	16.7	N/A	N/A	
1.12	1.1	1.03	1.05	-	-	11.6	N/A	N/A	
1.09	1.07	1.03	1.05	-	-	11.3	N/A	N/A	
1.07	1	0.96	0.95	-	-	13.3		142	169
1.12	1.1	1.11	1	-	-	11.8	N/A	N/A	
1.05	1.03	1.05	1.09	-	-	12.6	N/A	N/A	
1.07	1.01	1.05	1.05	-	-	12.3	N/A	N/A	
0.98	1.08	0.98	0.94	-	-	13.4	N/A	N/A	
1	1.01	1.03	1.06	-	-	16.2	N/A	N/A	
0.98	1.03	1.05	1.06	-	-	11.1	N/A	N/A	
1.04	1.04	1.06	1.03	-	-	12.6	N/A	N/A	
1.03	1	0.96	0.98	-	-	16.1		187	67
1.01	0.95	0.95	0.94	-	-	13.6	N/A	N/A	
0.94	1	0.95	0.93	-	-	11.6		149	99
1.05	1.06	1	1	-	-	11.7		205	295
1.04	0.99	0.99	0.97	-	-	14.4	N/A	N/A	
1.02	1	1.05	1	-	-	13.6	N/A	N/A	
1.08	1.09	1	1.08	-	-	12.5	N/A	N/A	
1	1.03	1.05	1.05	-	-	13.3	N/A	N/A	
1.02	0.96	1	1.02	-	-	13.1	N/A	N/A	
1.04	1.04	0.97	1.02	-	-	12.5	N/A	N/A	
1.09	1.1	1.07	1.07	-	-	11.5	N/A	N/A	
1	1	0.95	0.97	-	-	10	N/A	N/A	
1.07	1.09	1	1.04	-	-	14.3		259	56
1.07	1.06	1.07	1.04	-	-	15.7		197	155
1.07	1.05	1.06	1.04	-	-	14.3	N/A	N/A	
1.05	0.98	0.98	0.95	-	-	13.3	N/A	N/A	
0.98	1.06	0.93	0.96	-	-	12.9		138	322
1.03	1.08	1	1	-	-	11.8	N/A	N/A	
1.02	1.03	1.03	0.99	-	-	15.7		226	122
0.98	0.95	1.02	1	-	-	13.8	N/A	N/A	
1.02	1.03	1.03	0.94	-	-	12.2	N/A	N/A	
1.03	1.04	0.96	0.99	-	-	13.4	N/A	N/A	
0.94	1.09	0.91	1	-	-	10		98	55

0.93	0.92	0.92	0.9 -	-	10.7	N/A	N/A	
1.04	1.07	0.98	0.93 -	-	9.2	N/A	N/A	
0.97	1.03	0.97	0.94 -	-	11.6		146	53
1.07	1.03	1.06	1.02 -	-	11.1	N/A	N/A	



HDL	LDL	CD4	ALBUMIN	PAOD?	
	56	153	921	3.8	0
N/A	N/A		1096	2.8	0
N/A	N/A		369	4.8	0
	50	128	260	3.3	0
N/A	N/A		359	4.2	1
	23	72	511	4.3	0
	32	139	686	4.2	0
N/A	N/A		241	3.9	0
N/A	N/A		468	3.4	0
	51	104	502	4.6	0
N/A	N/A		281	4.3	1
N/A	N/A		544	N/A	1
	53	133	98	3.9	1
N/A	N/A		187	2.4	1
	26	57	280	4.3	1
N/A	N/A		315	2.9	0
	61	173	203	4.8	0
N/A	N/A		398	3.4	0
N/A	N/A		426	3.9	1
	17	103	493	4.9	0
N/A	N/A		579	5	1
	33	94	448	4.2	0
	42	108	202	3.5	0
	29	107	530	3.3	0
N/A	N/A		420	4.1	0
N/A	N/A		166	3.9	0
N/A	N/A		643	4.2	0
	70	141	465	4.5	0
N/A	N/A		170	3.4	0
N/A	N/A		155	4.4	0
N/A	N/A		499	5.1	0
	28	39	345	4.3	0
	19	54	315	3.7	0
N/A	N/A		295	3.4	0
N/A	N/A		1179	3.7	0
	40	151	306	N/A	0
N/A	N/A		198	4.4	1
N/A	N/A		194	3.7	0
N/A	N/A		127	2.8	0
	22	94	236	3.9	0
	33	81	670	4	0
N/A	N/A		73	3.9	0
N/A	N/A		315	2.9	0
N/A	N/A		57	4.5	0
N/A	N/A		231	2.1	0
N/A	N/A		206	3.2	0
N/A	N/A		675	N/A	0
N/A	N/A		430	4.8	0
N/A	N/A		484	4.3	0

	26	117	317	2.6	0
	41	99	409	2.8	0
N/A	N/A		339	4.4	0
N/A	N/A		503	4	0
N/A	N/A		268	N/A	0
N/A	N/A		287	5.1	0
N/A	N/A		534	N/A	1
N/A	N/A		381	2.6	0
	38	103	452	4.8	0
N/A	N/A		297	4.5	0
N/A	N/A		222	3.8	1
	41	96	484	5	0
	59	96	114	3.7	0
	29	77	527	3.4	0
N/A	N/A		271	3.7	0
N/A	N/A		299	3.2	0
N/A	N/A		204	4.7	0
	35	143	278	4.5	1
	31	123	330	4.1	0
	34	74	698	3.4	0
N/A	N/A		465	3.9	0
N/A	N/A		206	4.6	0
N/A	N/A		349	3.5	1
	27	93	528	4.9	0
	43	71	177	N/A	0
N/A	N/A		164	3.4	0
	31	111	257	4.8	0
N/A		41	317	4.7	0
N/A	N/A		454	3.1	0
N/A	N/A		116	4.4	0
	12	101	314	2	0
N/A	N/A		190	3.3	0
	30	100	15	3.8	0
N/A	N/A		275	4.1	0
	31	72	333	4.4	0
N/A	N/A		965	4.9	0
	38	108	36	4.3	0
N/A	N/A		639	3.3	0
	43	115	344	4.1	0
N/A	N/A		170	3.4	0
N/A	N/A		367	3.6	0
N/A	N/A		1002	N/A	0
	20	57	170	4.1	0
	39	113	66	1.8	0
N/A	N/A		120	2.7	0
	26	50	488	4.5	0
N/A	N/A		185	3.5	0
N/A	N/A		136	3	0
N/A	N/A		112	2.9	0
N/A	N/A		74	3	0

	27	115	325	4.5	0
	28	63	1055	4.2	0
N/A	N/A		543	3.8	0
N/A	N/A		175	4.3	0
N/A	N/A		139	4.2	0
	41	142	1129	4.7	0
	23	83	398	4.8	0
N/A	N/A		140	3.7	0
N/A	N/A		388	4.3	0
	27	87	673	4	0
N/A	N/A		611	3.6	0
N/A	N/A		710	4	0
N/A	N/A		353	3.7	0
N/A	N/A		610	3.7	1
N/A	N/A		592	3	0
N/A	N/A		468	4.7	0
N/A	N/A		449	4.2	0
N/A	N/A		248	3.7	0
N/A	N/A		383	4.1	1
N/A	N/A		804	4	0
N/A	N/A		688	3.5	0
N/A	N/A		688	3.5	0
	28	39	345	4.3	0
	49	110	582	4.9	0
N/A	N/A		605	4.1	0
	31	86	474	4.6	0
	28	95	874	4.9	0
N/A	N/A		148	3.3	0
N/A	N/A		639	3.3	0
N/A	N/A		662	3.2	0
	30	43	215	2.9	0
N/A	N/A		323 N/A		0
	25	66	164	3.4	0
N/A	N/A		315	4.6	0
	31	92	446	4.5	0
N/A	N/A		204	4.2	0
N/A	N/A		636	3.8	0
N/A	N/A		154	3.5	0
N/A	N/A		757	4	0
N/A	N/A		734	4.3	0
N/A	N/A		262	4.5	0
N/A	N/A		776	4.5	0
	31	54	406	3.6	0
N/A	N/A		321	4	0
N/A	N/A		337	3.8	0
N/A	N/A		626 N/A		0
	49	74	377	5.2	0
N/A	N/A		210	4.8	1
N/A	N/A		684 N/A		0
N/A	N/A		840 N/A		0

N/A	N/A		422	4	0
	30	55	144	4.1	0
	47	128	537	4.8	0
N/A	N/A		498	3.5	0
	28	58	378	4.3	0
N/A	N/A		710	4.3	1
N/A	N/A		381 N/A		0
N/A	N/A		21	4.4	0
N/A	N/A		643	4.6	0
N/A	N/A		1363	4.3	0
N/A	N/A		729 N/A		0
N/A	N/A		932	4.5	0
N/A	N/A		426 N/A		0
	37	90	460	4.7	0
	61	124	861 N/A		0
N/A	N/A		298	3.8	0
N/A	N/A		749	3.7	0
N/A	N/A		1213	4.9	0
	35	65	370 N/A		0
N/A	N/A		73	4.5	0
	35	101	940	4.4	0
N/A	N/A		172	4.6	0
N/A	N/A		1	2.4	0
N/A	N/A		720	4.6	0
N/A	N/A		577 N/A		0
	40	107	538	4.6	0
N/A	N/A		421 N/A		0
N/A	N/A		378 N/A		0
N/A	N/A		137	4.6	0
N/A	N/A		266	4.2	1
	40	109	586 N/A		0
N/A	N/A		580 N/A		0
N/A	N/A		498	3.4	0
	20	99	671 N/A		0
	76	91	391 N/A		0
N/A	N/A		499	4.2	0
N/A	N/A		346 N/A		1
N/A	N/A		111	2.8	0
	47	154	622	3.9	0
	21	72	702	4.3	0
N/A	N/A		339 N/A		0
	52	116	877		0
	57	105	234		0
N/A	N/A		565 N/A		0
N/A	N/A		223	4.8	0
N/A	N/A		432 N/A		0
N/A	N/A		484	3.4	1
	55	109	887	4.8	0
N/A	N/A		1137 N/A		0
N/A	N/A		368 N/A		0

N/A	N/A		467 N/A		0
N/A	N/A		380	2.4	0
N/A	N/A		709 N/A		1
N/A	N/A		101	3.2	0
N/A	N/A		229	3.7	0
N/A	N/A		80	4.2	0
N/A	N/A		565 N/A		0
N/A	N/A		635	4.5	0
N/A	N/A		1012	3.7	0
N/A	N/A		848	4.4	0
N/A	N/A		859	3.2	0
N/A	N/A		522 N/A		0
N/A	N/A		515 N/A		0
N/A	N/A		589 N/A		0
N/A	N/A		355	3.8	0
N/A	N/A		139	3.2	0
	31	136	751	4.2	0
	36	112	267	3.5	0
	52	98	282	4.2	0
	30	95	558	5.1	0
N/A	N/A		418	3.6	0
N/A	N/A		101 N/A		0
N/A	N/A		567 N/A		0
N/A	N/A		310	4.9	0
N/A	N/A		383	4.8	0
N/A	N/A		378 N/A		0
N/A	N/A		1021	4.6	0
N/A	N/A		586	4.3	0
N/A	N/A		679	5	0
N/A	N/A		503 N/A		0
N/A	N/A		1158	4.1	0
N/A	N/A		553	3.5	0
N/A	N/A		460	3.4	0
	35	101	912	4.9	0
	33	99	448	3.7	0
	57	151	423 N/A		0
	37	89	688	4.1	0
N/A	N/A		772 N/A		0
N/A	N/A		287	3.3	0
N/A	N/A		631 N/A		0
N/A	N/A		367 N/A		0
	35	77	572	3.2	0
N/A	N/A		673	4	0
N/A	N/A		539 N/A		0
N/A	N/A		389 N/A		0
	33	81	304	4	1
N/A	N/A		681 N/A		0
N/A	N/A		492 N/A		1
N/A	N/A		259	3.5	0
N/A	N/A		196	4.9	0

N/A	N/A		358	4.6	0
N/A	N/A		557	3.7	0
N/A	N/A		230	2.3	0
N/A	N/A		276	3.9	0
N/A	N/A		345	N/A	0
N/A	N/A		497	3	0
N/A	N/A		58	4.2	0
N/A	N/A		552	N/A	0
N/A	N/A		343	3.4	0
N/A	N/A		1006	N/A	0
N/A	N/A		405	4	0
N/A	N/A		667	4.3	0
	42	94	639	4.1	0
	40	141	544	N/A	0
	27	125	283	3.3	0
N/A	N/A		441	N/A	0
N/A	N/A		224	3.5	0
N/A	N/A		603	4	0
N/A	N/A		1065	N/A	0
N/A	N/A		592	4	0
N/A	N/A		208	3.8	0
	35	96	1006	3.7	0
N/A	N/A		449	3.9	1
N/A	N/A		496	N/A	0
N/A	N/A		841	4.1	0
	24	52	437	N/A	0
N/A	N/A		500	3.7	0
N/A	N/A		28	N/A	0
	30	47	216	4.9	0
N/A	N/A		600	N/A	0
	49	119	452	3.7	0
N/A	N/A		501	4.2	0
N/A	N/A		431	4.9	0
N/A	N/A		116	4.4	0
N/A	N/A		647	4.5	0
N/A	N/A		409	4.5	0
N/A	N/A		479	N/A	0
N/A	N/A		177	3.9	0
N/A	N/A		980	5	0
N/A	N/A		980	N/A	0
N/A	N/A		1032	N/A	0
N/A	N/A		413	3.2	0
N/A	N/A		327	N/A	0
N/A	N/A		745	N/A	0
N/A	N/A		956	N/A	0
	38	100	1231	4.1	0
N/A	N/A		294	4.5	0
N/A	N/A		118	N/A	0
N/A	N/A		519	N/A	0
N/A	N/A		338	3.4	0

	30	102	212	3.1	1
N/A	N/A		529 N/A		0
N/A	N/A		193	2.1	0
N/A	N/A		268	4	0
N/A	N/A		497	3.7	0
N/A	N/A		89	3.9	0
	27	58	110	4	0
N/A	N/A		4	2.1	1
N/A	N/A		59	3.3	1
	37	78	821 N/A		0
N/A	N/A		777 N/A		0
N/A	N/A		696	4.7	0
	30	49	502	4.1	0
N/A	N/A		519	3.8	0
	40	108	457	4.1	0
N/A	N/A		230 N/A		0
N/A	N/A		359 N/A		0
N/A	N/A		277 N/A		0
	63	120	372	4.6	1
N/A	N/A		269 N/A		0
	39	84	301	3.9	0
N/A	N/A		439 N/A		0
N/A	N/A		325	4	0
N/A	N/A		471 N/A		0
N/A	N/A		207	4.3	1
N/A	N/A		996 N/A		0
N/A	N/A		483	3.5	0
N/A	N/A		258	4.2	0
	40	102	277 N/A		1
N/A	N/A		629	4.5	0
N/A	N/A		313	4.2	0
N/A	N/A		547 N/A		0
N/A	N/A		117	3.1	1
N/A	N/A		527	3.6	0
	32	100	315	4	1
N/A	N/A		797 N/A		0
N/A	N/A		614 N/A		0
N/A	N/A		286 N/A		0
N/A	N/A		152	4.7	0
N/A	N/A		297	4.2	0
N/A	N/A		392 N/A		0
N/A	N/A		552 N/A		0
N/A	N/A		192	4.7	0
N/A	N/A		205	4.6	0
N/A	N/A		202	4.3	0
N/A	N/A		482	4.7	0
N/A	N/A		795	4.7	0
N/A	N/A		243 N/A		0
N/A	N/A		497 N/A		0
N/A	N/A		609 N/A		0

N/A	N/A		637	N/A	0
N/A	N/A		1018	N/A	0
	52	110	693	N/A	0
N/A	N/A		801	N/A	0
N/A	N/A		465	N/A	0
N/A	N/A		293	N/A	0
N/A	N/A		278	2.3	0
N/A	N/A		882	N/A	0
N/A	N/A		364	3.6	0
N/A	N/A		781	N/A	0
N/A	N/A		366	4.5	0
	39	71	537	4.3	0
N/A	N/A		656	N/A	0
	51	110	627	N/A	0
N/A	N/A		138	N/A	0
N/A	N/A		568	2.3	0
N/A	N/A		76	N/A	0
N/A	N/A		936	N/A	0
N/A	N/A		410	3.6	0
	22	95	112	4	0
N/A	N/A		715	N/A	0
N/A	N/A		250	4.8	0
N/A	N/A		343	3.7	0
N/A	N/A		598	N/A	0
N/A	N/A		509	N/A	0
N/A	N/A		298	4.4	0
N/A	N/A		673	N/A	0
	62	108	592	N/A	0
N/A	N/A		515	N/A	0
	34	103	559	4.4	0
	36	132	247	N/A	0
N/A	N/A		687	N/A	0
N/A	N/A		404	4.2	0
N/A	N/A		790	4.1	0
N/A	N/A		566	N/A	0
N/A	N/A		623	N/A	0
N/A	N/A		328	4.3	0
N/A	N/A		826	N/A	0
N/A	N/A		432	3.4	0
	40	106	328	4.9	0
	52	135	375	N/A	0
N/A	N/A		517	N/A	0
N/A	N/A		728	N/A	0
	20	71	42	4.2	0
N/A	N/A		53	6.3	0
	65	127	518	4.7	0
N/A	N/A		125	4.3	0
N/A	N/A		1072	3.8	0
N/A	N/A		3	4.5	0
	29	55	35	2.8	0



N/A	N/A		691	N/A	0
N/A	N/A		757	3.3	0
	36	101	344	4.4	0
N/A	N/A		525	3.7	0